UNIVERSITY OF THE WESTERN CAPE

PAEDIATRIC SEVERE-ACUTE MALNUTRITION AND THE RECOMMENDED *W.H.O* TREATMENT MODALITY: AN EPIDEMIOLOGICAL AND QUALITY CARE ASSESSMENT IN THE CONTEXT OF HIV/AIDS COMORBIDITY

By

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A thesis submitted in fulfilment of the requirements for the awarding of a DOCTOR OF PHILOSOPHY Degree in Public Health at the School of Public Health in the Faculty of Community and Health Sciences, University of the Western Cape

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DECLARATION

I declare that "***Paediatric Severe – Acute Malnutrition and the recommended WHO treatment modality: An epidemiological and quality care assessment in the context of HIV comorbidity***" is my own work, that it has not been submitted for any degree or examination in any other university, and that all the sources used or quoted have been indicated and acknowledged by means of complete references.

Signature_____ **Date 28-08-2015**

DEDICATION

To my wife Germaine Muzigaba, my daughter Iriza Aviella Muzigaba, my parents, and my siblings Clarisse, Claire and Carlos: Your love and support during this journey has been incredible.

To all hardworking adults out there who strive to get an education despite being surrounded by multiple family and work-related responsibilities

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LIST OF ACRONYMS

AIDS	Acquired Immune Deficiency Syndrome
CFR	Case Fatality Rate
CI	Confidence Interval
DCSTs	District Clinical Specialist Teams
FGD	Focus Group Discussion
HCT	HIV Counselling and Testing
HIV	Human Immunodeficiency Virus
IRR	Incidence Rate Ratio
IV	Intravenous Fluid
MMD	Mixed Methods Design
MUAC	Mid-Upper Arm Circumference
OR	Operational Research
PCA	Principal Component Analysis
RR	Risk Ratio
SAM	Severe Acute Malnutrition
TB	Tuberculosis
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNHCR	United Nations High Commission for Refugees
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
UWC	University of the Western Cape
WHO	World Health Organisation

ABSTRACT

Introduction

The current study was, in part, prompted by the high case fatality rates for severe acute malnutrition in two district hospitals in the Eastern Cape Province in South Africa. These case fatality rates were being attributed to Human Immunodeficiency Virus infection rather than to mismanagement by nurses involved in the hospital management of SAM cases. There were also some anecdotes from clinicians in the same hospitals that, depending on the clinical stage of HIV infection, the World Health Organisation's ten-step protocol may show no effect. This left some uncertainties as to whether these guidelines are suitably designed for use during the management of HIV positive children who are severely malnourished and at different HIV clinical stages. This study sought to reinforce the design of a longstanding facility-based intervention originally developed to improve the management of severe acute malnutrition in two district hospitals in South Africa. The aim was to design an improved intervention which was implemented and evaluated to determine its potential effect on treatment outcomes, specifically in the context of high HIV comorbidity. The study also sought to provide the context for the effectiveness of this intervention, in terms of its implementation fidelity and associated moderating factors. Lastly, the study evaluated the sustainability of the intervention after it was discontinued.

Methods

The current study reports on the development, implementation and evaluation of an intervention to improve the management of severe acute malnutrition in two district hospitals in the Eastern Cape Province. A Sequential Explanatory Mixed Method Design was used. During the study, the effect of HIV infection, disease stage and other clinical characteristics on the survival of children with severe acute malnutrition was assessed. The relationship between the rate of weight gain and duration of hospitalisation based on HIV status and disease stage were also examined. The data were collected prospectively during the study using

retrospective record review of a total of 450 severely malnourished children who were admitted and treated at the two facilities from 2009 to 2013. A pre-tested 76-item patient evaluation form was used to collect data on patient characteristics on admission, treatment processes and outcomes. Data analysis was performed using STATA 13.0 and involved simple descriptive computation of quantitative variables as well as non-parametric tests to compare groups between and within hospitals. Kaplan-Meier curves and Cox proportional hazard modelling were used to analyse time to event data. The study also assessed the impact of the intervention at time intervals on outcomes of interest. The analysis focused on modelling and plotting monthly mortality statistics collected over a period of 69 months. This was done to detect related trend and level changes before, immediately (after the first two months) and after (following the two months) the removal of the intervention. Lastly ethnographic and focus group enquiries were used to explain the quantitative results. Two focus group discussions were held in each hospital with clinicians and the management staff. This was done at the end of phase three. The focus group data were analysed using the framework analysis approach.

Findings

HIV positive SAM cases had worse survival prospects than their HIV negative counterparts over the study period (AHR=5.64; $p<0.001$). Compared to earlier stages of HIV infection, survival was poorer for HIV positive SAM cases that were at stage 3 and 4 at admission (AHR=5.47; $p<0.001$ and AHR=6.84; $p<0.001$ respectively). HIV status and case severity at admission were the strongest independent predictors of death, both in the adjusted and unadjusted models. Being critically ill and having lower respiratory tract infection were, both independently and as a combination, potential effect modifiers of higher risk of death. Cases that were HIV negative generally recorded a better rate of weight gain than their HIV positive counterparts (Median=7.5 vs. 3.6g/kg/day respectively). There were no difference between HIV positive and HIV negative cases with regard to duration of hospitalisation among those who were discharged. The median rate of weight gain got smaller with advanced HIV disease stage, whereas the median duration of hospitalisation became

longer. The impact of the intervention was generally sustainable in improving the three mortality indicators of severe acute malnutrition (Total mortality attributable to severe acute malnutrition, severe acute malnutrition death within 24 hours of admission and Mortality attributable to severe acute malnutrition and HIV infection) after it was discontinued . However, the total severe acute malnutrition mortality worsened every month after the discontinuation of the intervention at Holy Cross hospital.

The qualitative enquiry highlighted additional factors which were believed by health care workers to contribute to high case fatality rates for severe acute malnutrition. These ranged from the antecedents of critical illness such as traditional medical use and household negligence, to high HIV prevalence associated with lack of status disclosure and poor adherence to antiretroviral therapy which resulted in virological failure, misdiagnosis at the first point of care, hospital-level expertise to deal with complex presentations, as well as sporadic gaps in the skilled workforce and resources to sustain the quality of care.

Conclusion

The study confirmed the findings from previous studies that HIV infected severely malnourished children have worse survival prospects, poorer nutritional recovery than their HIV uninfected counterparts when they are all treated according to the world health organisation guidelines implemented in the context of an implementation research project. The new finding from this study was that these outcomes differ at different stages of HIV infection among cases that were put on antiretroviral therapy using standard guidelines. The revision of the guidelines to address the effect of HIV infection on treatment outcomes becomes imperative. The study also showed that there were some facility-based and system-wide challenges associated with the implementation of the World Health Organisation guidelines. These need to be addressed holistically through concerted efforts by government, civil society and community-based organisations,

Key words

HIV, disease stage, epidemiology, hospital, severe acute malnutrition, survival, rate of weight gain, duration of hospitalisation, intervention, sustainability

CHAPTER 1

INTRODUCTION

1.1. Background

Malnutrition, in its various forms, remains a major public health problem (Collins, 2007). According to the United Nations Children's Fund (UNICEF, 2007), about 35% of the 7.6 million deaths that occur each year among children who are under 5 years of age, are due to nutrition-related factors (UNICEF, 2012). About 5% of such deaths are specifically attributable to severe wasting which results from acute undernourishment (Black et al., 2013). The World Health Organisation (WHO) estimates this condition to be affecting 19 million preschool-age children, mostly from the WHO African Regions and South-East Asian Region (WHO, 2013). Stunting, on the other hand, has been regarded as a much more concerning public health problem than wasting as it more accurately reflects nutritional deficiencies and illness that occur during the most crucial phases of childhood growth and development (UNICEF, 2009). Interestingly, South Africa is also among the 24 countries which account for more than 80% of the worldwide burden of stunting (UNICEF, 2009).

Before the 1970s, estimates for facility-based case fatality rates for severe acute malnutrition (SAM) in resource-constrained settings ranged between 20% and 30% for marasmus and up to 50-60% for Kwashiorkor (Cook, 1971; Schofield, Ashworth, 1997). A review of treatment practices worldwide found that many health services used outdated practices and that staff were unfamiliar with modern and effective guidelines for the management of severe malnutrition (Schofield, Ashworth, 1997). Inappropriate practices associated with high mortality included, amongst other things, poor knowledge of the health care givers, overuse of intravenous (IV) fluids

for rehydration, inadequate feeding leading to hypoglycaemia and hypothermia, untreated infections, and failure to correct electrolyte and micronutrient deficiencies (Schofield, Ashworth, 1997). Slow recovery among survivors has been shown to be associated with insufficient provision of energy and nutrients necessary for rapid catch up growth (Schofield, Ashworth, 1996). Staff's attitudes towards severely malnourished children have also been found to affect the outcome in these children (Puoane et al., 2006).

In an effort to reduce deaths from SAM and improve recovery, the World Health Organization (WHO) developed "Ten steps" guidelines for managing SAM (WHO, 1999 & WHO, 2000). These guidelines have since been promoted as the standard approach for clinical care of severely malnourished children under the age of 5 years. These guidelines are now being used in most health care units around the world, including some hospitals in South Africa (Puoane et al., 2001).

More recently, the WHO commissioned a task team to revise and update the ten-step guidelines which have been in existence for many years past (WHO, 2013). The update focused on eight specific areas, including: admission and discharge criteria, management of oedematous SAM cases, use of antibiotics, vitamin A supplementation, therapeutic feeding approaches, fluid management, management of HIV co-infection and case identification (WHO, 2013). This update put forward by the WHO, however, do not include all the aspects of the WHO guidelines for the management of SAM. The focus was only on areas which were prioritised by the guideline-development group (WHO, 2013). Therefore, this exercise was a preliminary phase in the process of updating the already-existing manual for

physicians and other senior health workers which has been in use for over a decade and half.

In hospitals where the original WHO treatment guidelines for SAM have been implemented, it has been shown that when quality care and resources (both human and material) were available, case fatality rates (CASE FATALITY RATEs) were dramatically reduced (Cavalcante et al., 1998; Ashworth et al., 2004; Deen et al., 2003; Ahmed et al., 1999). There is evidence to show that CASE FATALITY RATEs may improve from around 40% to less than 10 % (Wilkinson, Scrace, Boyd, 1996), even when the guidelines are used in emergency humanitarian interventions (Prudhon et al, 1996 & Grelley, 2000). However, disparities in treatment outcomes in various treatment centres across the developing world have been reported. While some centres have recorded less than 5% case fatality rates, others, including some hospitals in South Africa performed poorly with a CASE FATALITY RATE of approximately 50% (Puoane et al., 2001).

1.2. Problem Statement

1.2.1. Severe Acute Malnutrition in the context of HIV infection

The current study was, in part, prompted by the high CASE FATALITY RATEs for SAM in two district hospitals in the Eastern Cape Province in South Africa. Here, the high CASE FATALITY RATEs were being attributed to HIV infection rather than to mismanagement by nurses involved in the hospital management of SAM cases. There were also some anecdotes from clinicians in the same hospitals that, depending on the clinical stage of HIV infection, the WHO ten-step protocol may

show no effect. This left some uncertainties as to whether the WHO ten-step guidelines are suitably designed for use during management of HIV positive children who are severely malnourished and at different HIV clinical stages.

Furthermore, on a much broader scale, evidence on the potential effect of HIV infection on survival of children with SAM remains inconclusive due to lack of evidence. It remains unclear whether survival prospects are similar between HIV infected and HIV uninfected children with SAM who are treated exclusively and presumably equally, according to the WHO 10-step guidelines. This gap in knowledge poses some concerns considering that HIV/AIDS, which is staggeringly affecting Sub-Saharan Africa, has changed the face of childhood malnutrition in terms of malnutrition prevalence and incidence rates. Also, to our knowledge, there are very few studies which have investigated whether the different HIV clinical stages may have varying effects on survival of severely malnourished children with HIV infection who have been treated according to the WHO guidelines.

The few studies which have thus far investigated the relationship between HIV infection and SAM among children have focused mainly on differences in clinical features and haematological characteristics (Bachou et al., 2006; Prazuck et al., 1993; Mgone et al., 1991; Ticklay et al., 1997). Other studies have reported the use of either other therapeutic methods (Chinkhumba et al., 2008; Ndekha et al., 2004) or a slight modification of the standard WHO 10-step guidelines (De Maayer and Salloojee, 2011) in order to assess the effect of HIV infection on survival prospects of study subjects. Generally, the studies reported conflicting evidence across specific outcomes of interest.

In South Africa, the study by Maayer and Saloojee (2001) was the first of its kind to model the effect of co-infection of HIV and Tuberculosis (TB) on survival of children with SAM who were treated according to a slightly modified WHO treatment protocol. The comorbidity of HIV and TB infections in children under the age of five years has of late been a major public health concern. This is primarily due to the fact that the dual infection has led to an epidemic of *secondary* SAM. Secondary SAM is more associated with poor outcomes than *primary* severe malnutrition which is due to insufficient nutrient intake and non-HIV/TB related infections (Heikens, 2007). Evidence on the impact of this dual infection on survival of children with SAM in the context of the WHO treatment modality also remains low (Heikens, 2007).

1.2.2. HIV infection, the rate of weight gain and duration of hospitalisation

According to Fergusson et al. (2009), few studies have reported on nutritional recovery and survival among severely malnourished children with HIV infection. Researchers who have attempted to explore this relationship have mostly found inconsistent findings which were generated from varied methodological approaches (Fergusson et al., 2009). Some studies have reported similar nutritional recovery between HIV positive and negative SAM cases (Ndekha et al., 2005 and Fergusson et al., 2009), while others have not (Sandige et al., 2004). The evidence around this phenomenon therefore remains inconclusive to a certain degree.

Furthermore, the recent WHO update of the WHO guidelines (WHO, 2013) also highlights the existing gap in knowledge regarding nutritional recovery among children with SAM who are HIV infected and are treated according to the current

WHO treatment modality. Despite "very low quality" evidence of causal effect, the WHO guidelines revision group recommends that children with SAM who are HIV infected should be managed using the same therapeutic feeding approaches irrespective of HIV status.

Also, there have been few studies to date in the literature which has investigated the relationship between duration of hospitalisation and the rate of weight gain, comparing HIV infected and uninfected SAM cases. Initial observations from the two hospitals in which this study was conducted revealed that children were being discharged without due regard to the rate of weight gain achieved before sending them off. This was, in part, because it was not clear to the health care workers how long the child needs to be in care in order to achieve optimal weight gain. An enquiry into this aspect of care was important particularly considering the insufficient resources available to provide prolonged care in both hospitals. There was also some speculation that HIV infected children would not gain weight at the same rate as their HIV uninfected counterparts no matter how well and for how long the guidelines were used to treat them. Therefore, advising health care workers on how long they should keep SAM cases on therapeutic feeds was critical.

As the nature of this study was operational, this was important not only to promote practices that lead to good nutritional recovery at ward level, but also to enable the hospital administrators and the clinical teams to make informed decisions regarding resource allocation based on the patient's condition.

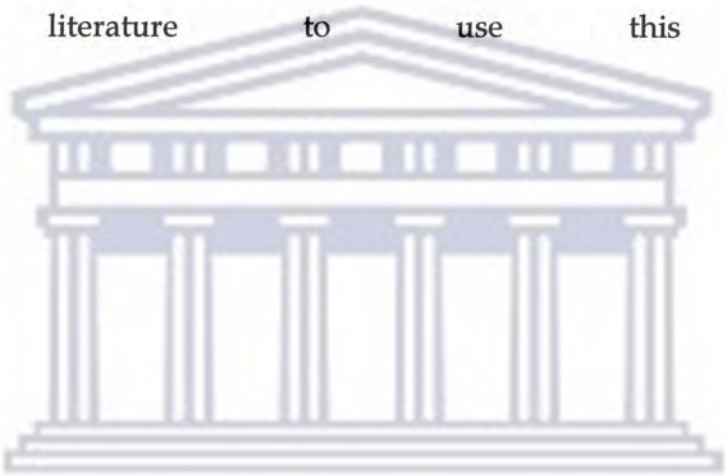
1.2.3. Sustainability of a facility based intervention to improve outcomes related to SAM

There is a wealth of evidence available in the literature on various methodological approaches that can be used to evaluate longitudinal effects of facility-based interventions to improve outcomes in various domains (Shadish, Cook and Campbell, 2002). Randomised controlled trials and the interrupted time series designs are some of the widely used rigorous impact evaluation designs (Cook and Campbell, 1979). However, the application of these methods in assessing the sustainability of facility-based nutrition rehabilitation interventions is still limited (WHO, 2013). In effect, methodologically rigorous studies that have specifically assessed the impact of discontinuing a structured facility-based intervention involving the WHO 10-step guidelines, on the sustainability of the SAM-related outcomes over time, remain undocumented. Most nutrition rehabilitation interventions implemented at either community or facility levels have used less rigorous methods such as cross sectional surveys, qualitative methods and some forms of quasi-experimental designs, in order to evaluate intervention sustainability (Collins, 2007).

The current study involved the design and implementation of a health systems strengthening intervention to improve SAM outcomes (See Chapter 3). The study was implemented over a number of years and discontinued at the end of the funding period. Although a number of support structures were put in place at the beginning of the intervention to sustain it, it was not clear whether the outcomes would

improve with the presence of the intervention or worsen in its absence, i.e. after the withdrawal of the support from the research team.

Ascertaining the sustainability of the intervention after its discontinuation was imperative to be able to investigate further some of the success factors, if any, that could be scaled up to other settings and also to explore the challenges that could be considered for future interventions. This study was the first of its kind in the documented literature to use this approach.



CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

This chapter reviews the relevant literature on paediatric SAM. But firstly, malnutrition and its various forms are described. Later on, the focus of the chapter shifts exclusively to SAM as a form of malnutrition and some of the methods used to screen this condition. The chapter continues with a discussion on the pathophysiological and metabolic changes associated with paediatric SAM. The burden of SAM locally and globally is highlighted, and the various treatment modalities used to manage SAM, particularly the WHO – ten-step guidelines and their effectiveness in the context of HIV infection, are also discussed. Current research gaps in the literature on SAM are discussed and a link is made to how this research has, in part, attempted to address some of these gaps. Finally, the chapter outlines and compares theoretical underpinnings of this study and how these were used to frame the relevant research methodologies.

2.2. Defining malnutrition and its various forms

Malnutrition includes both undernutrition and obesity (Mehta et al. 2013). However, for the sake of this study, only undernutrition and its various forms are discussed. The definitions will also focus only on undernutrition among children below the age of six years (hereinafter referred to as paediatric undernutrition and later, paediatric severe acute malnutrition) and in the context of the developing world.

2.2.1. Paediatric undernutrition

Paediatric undernutrition is defined as an imbalance between nutrient intake and nutrient requirements which, when not corrected, results in progressive deficits of

energy, protein, micronutrients and some forms of electrolytes in the body (Mehta et al. 2013). The deficit of these nutrients in the body may negatively affect long-term health outcomes such as growth and development and the overall quality of life during adulthood. Adverse short-term outcomes such as inability to thrive and lack of immunological integrity may also result (Mehta et al. 2013).

Paediatric malnutrition can be a result of one or multiple aetiological processes such as illness (one or more diseases or injuries), social and environmental factors (poverty and natural disasters) which are associated with decreased nutrient intake or delivery or both (Joosten and Hulst, 2008 & Mehta et al., 2013). More recent scientific breakthroughs have also begun to recognise the disease-related paediatric undernutrition which results from inflammation (Jensen, 2010).

Paediatric undernutrition can be classified as acute (duration of less than 3 months) or chronic (duration of three months or longer) (Gomez et al., 2000). Under chronic conditions, undernutrition may lead to diminished growth velocity (stunting), whereas under acute conditions the most common outcome is wasting. The conditions may also be mild (z-score <-1), moderate (z-score between -2 and -3) and severe (z-score <-3) (WHO, 2006). Figure 2 below which was adapted from Mehta et al. (2013) outlines the aetiology of paediatric undernutrition in general, the possible mechanisms involved and some of the outcomes documented in the literature.

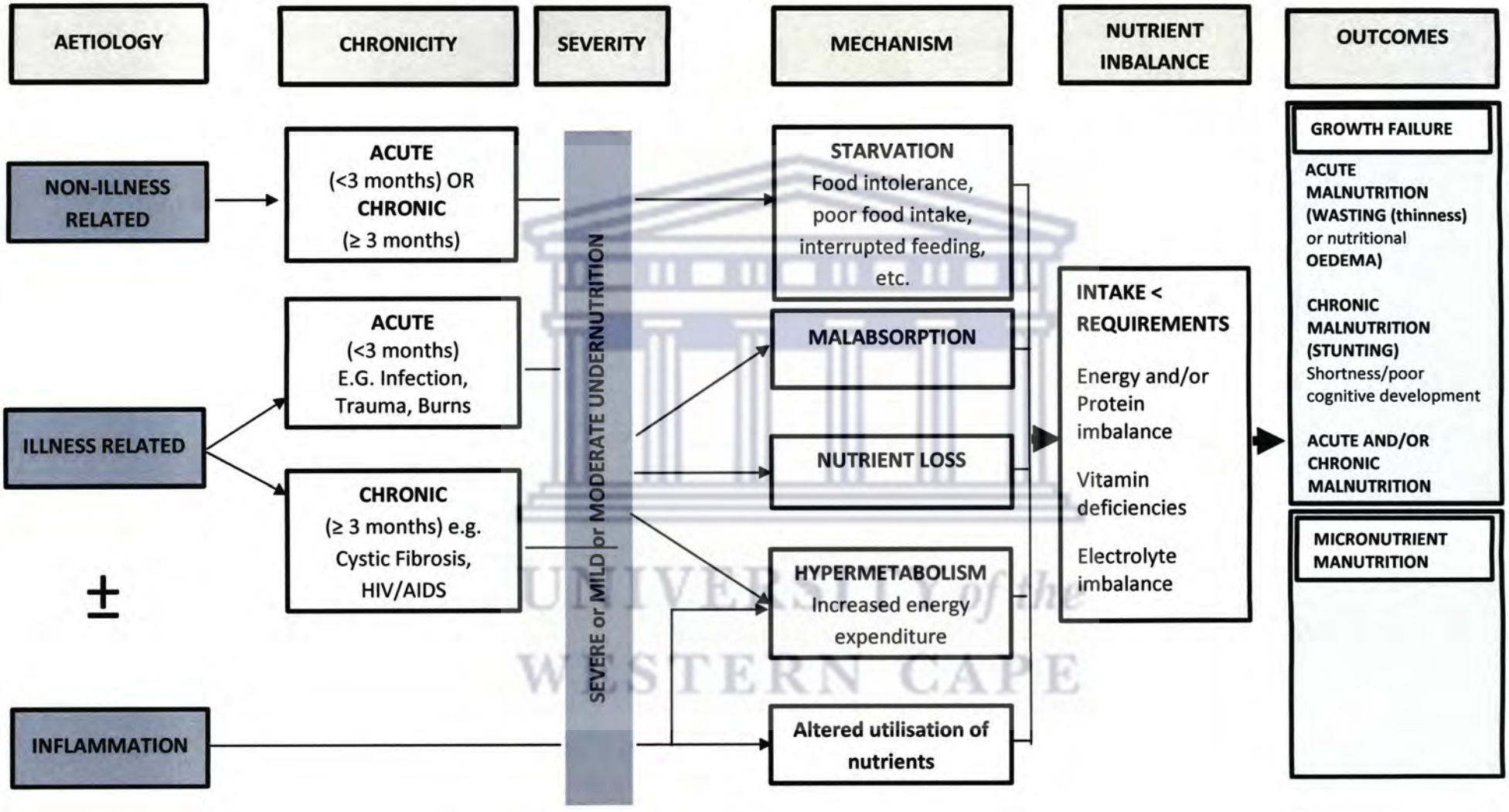


Figure 2: *Aetiology, chronicity, severity, mechanisms and outcomes in paediatric undernutrition*

The next sections of this chapter will focus solely on Paediatric Severe Acute Malnutrition which is a form of paediatric undernutrition and the main exposure investigated in this study.

2.2.2. Severe Acute Malnutrition: Definition and screening

Severe Acute Malnutrition is a form of acute under-nutrition which results from a relatively short duration of nutritional deficit (Collins, 2007). Advanced cases of acute undernutrition are complicated by concurrent infective illnesses, particularly acute respiratory infection, diarrhoea, and gram-negative septicaemia (Collins, 2006). The nutritional status of children can also be affected by chronic infections such as HIV (WHO, 2013). In the Southern African region, the prevalence of HIV in children with SAM has been estimated to be around 30% (UNAIDS, 2007; Fergusson, Tomkins, 2009) and 50% in other African regions (Amadi, 2001). Generally, children who suffer from SAM are prone to increased risk of morbidity and mortality, impaired cognitive development, suboptimal adult work capacity and increased risk of adulthood diseases (Black et al., 2013; Briend et al., 1989; Bairagi, 1981).

The WHO defines SAM in children who are 6-59 months of age as a weight-for-height less than -3 Z-score of the median of the WHO growth standard (WHO, 1999), or the presence of clinical signs of bilateral pitting oedema of nutritional origin (oedematous malnutrition) despite other measures being above specified cut-off values (WHO, 2009). Severe malnutrition has also been defined by the United Nations High Commission for Refugees (UNHCR) as a mid-upper-arm circumference (MUAC) of less than 110 mm in children aged 1–5 years. The MUAC

has been endorsed in the Joint United Nations Statement on management of SAM as an independent criterion for screening SAM both at facility and community levels (United Nations Joint Statement, 2007).

Severe acute malnutrition exists in three syndromic forms namely: marasmus, kwashiorkor and marasmic kwashiorkor. According to the UNICEF (2012) marasmus is generally characterised by severe weight loss or wasting of fat and muscle mass which the body breaks down to meet its increasing energy requirements. It is the most common form of SAM and can quickly lead to death if not identified soon and treated. Kwashiorkor, on the other hand, is characterised by a bloated appearance due to water retention which is clinically known as bilateral oedema. This severe accumulation of fluid in body tissues is largely a result of nutritional deficiencies. Nutritional oedema can be caused by insufficient protein intake resulting in hypoproteinemia and low plasma oncotic pressure. Oedema is also related to impairment of sodium potassium pump as a result of cellular damage thought to be due to various insults causing an excess of free radicals (Golden, 1998). Marasmic Kwashiorkor, though often difficult to identify by heath care workers, is characterised by both wasting and bilateral oedema. Both kwashiorkor and marasmic-kwashiorkor are also classified as SAM (UNICEF, 2012). The reason for difficulty in detecting Marasmic Kwashiorkor is because of the shared features from both kwashiorkor and marasmus which most health care workers do not always detect and end up defining the case as one or the other and not as marasmic kwashiorkor.

2.3. Global burden of and trends in childhood malnutrition

Towards the end of the year 2013, the UNICEF, the WHO and the Word Bank released new global and regional estimates of the burden of childhood malnutrition for the period 1990 to 2012 (UNICEF, 2013). According to the WHO summary of the main findings (WHO, 2014), estimates of the global burden of wasting and severe wasting indicate that in 2012 about 51 million under-five-year olds were wasted and 17 million were severely wasted. The prevalence of wasting and severe wasting was estimated at about 8% and 3% respectively in the same year. In 2012, about 70% of all severely wasted children lived in Asia and 28 % in Africa.

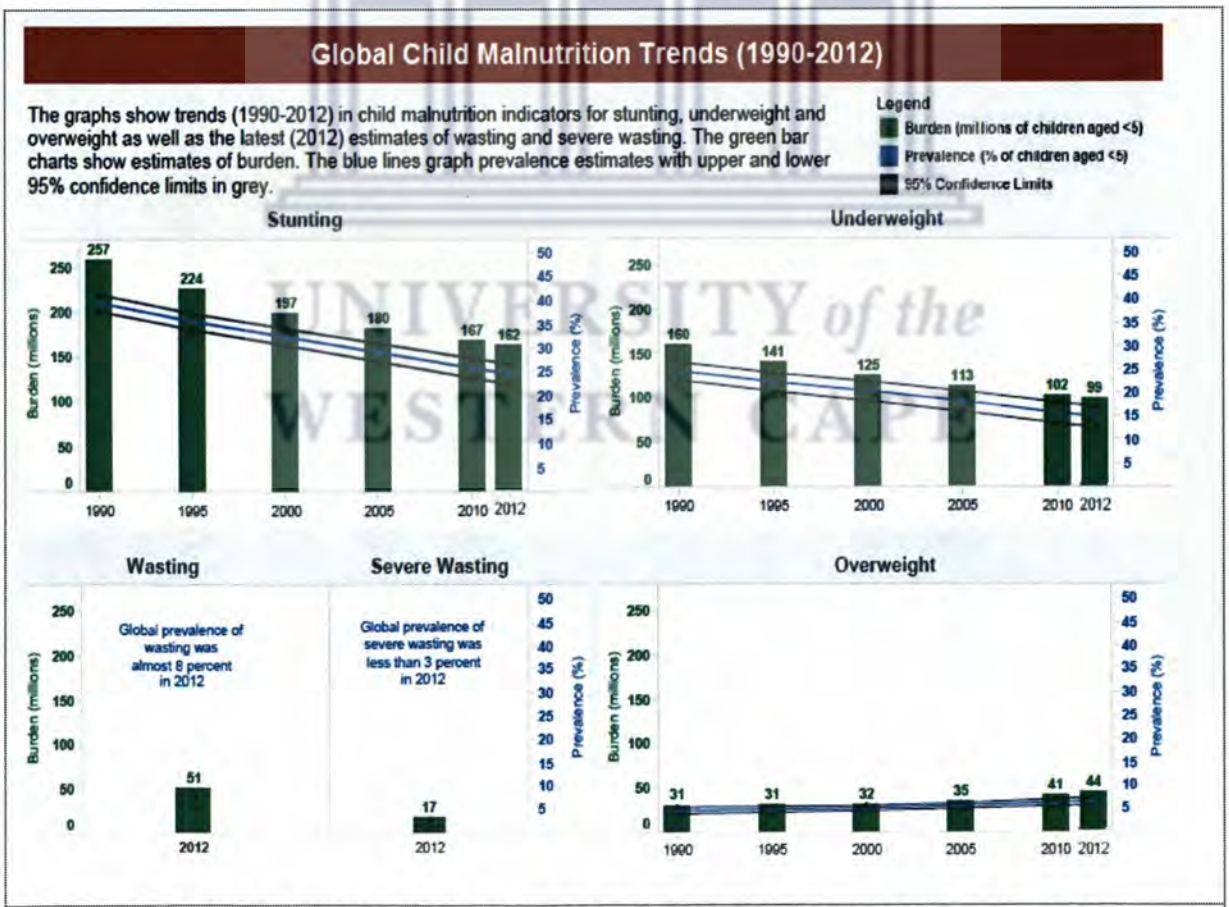


Figure 3: *UNICEF, WHO and the World Bank joint estimates of child malnutrition using available data up to 2012. Source: UNICEF, 2013*

The WHO summary also reported a global decline in the underweight prevalence between 1990 and 2012, which was from 25% to 15%. Close to 99 million under-five-year olds were underweight in 2012, of which 67 % lived in Asia and 29% in Africa. Overall, stunting presented the largest burden of undernutrition compared to underweight, wasting and severe wasting. In 2012, about 162 million children under the age of five years were stunted globally and Asia had the largest burden (56%) compared to Africa (36%). However, the global trend in stunting prevalence continues to decline and has moved from 33% in 2000 to 25% in 2012 but remains too high to meet the Millennium Development Goal target of halving the 1990 prevalence by 2015. Figure 3 below summarises some of the estimates reported in the UNICEF, WHO and World Bank joint report.

2.4. Tackling the global burden of SAM

Malnourished children are much more likely to die, with or without complications, than their well-nourished counterparts (Pelletier, 1995). They also do not respond to medical treatment the same way as well-nourished children (Jackson, Ashworth, 2006). Special guidelines for treating severely malnourished children are therefore required because of peculiar pathophysiological and metabolic changes that the body undergoes. Reductive adaptation which occurs in SAM requires specialised management and practitioners rehabilitating SAM cases should be aware of this delicate homeostatic mechanism (Waterlow, 1986).

2.4.1. Pathophysiological and metabolic changes in SAM

Mortality rates and poor weight gain in SAM can be substantially improved by modifying treatment in a way that takes into account the pathophysiological and metabolic changes associated with the condition. These changes affect every cell, organ and system of the patient (WHO, 1999) and treatment requires following specific steps and order. The WHO manual on principles of care for SAM (WHO, 2002) highlights some of the changes which occur in a severely malnourished child.

In most cases, the body systems begin to shut down in a phenomenon called "reductive adaptation". This phenomenon is marked by reduced homeostasis and is necessary as it enables the body to cut down energy expenditure, thereby allowing survival of the patient on limited calories (Waterlow, 2006). These changes are associated with selective decreased organ function particularly the heart, liver and kidney. There is often altered glucose metabolism, which increases the risk of hypoglycaemia and decreased cardiac output (Waterlow, 2006). The risk of fluid overload and heart failure are also heightened by decreased kidney ability to excrete extra fluid out of the system (Wilkinson, Scrace and Boyd, 1996). Feeding must thus be done slowly and cautiously as rapid feeding or provision of fluids may overwhelm the body's system. Also, as the child is treated, the body's systems must gradually learn to function fully (WHO, 2002).

Research has shown that nearly all children with SAM have bacterial infection though the usual signs of infection may not be apparent as a result of reductive adaptation (Cavalcante et al., 1998). In most cases, there is a weakened immune

function due to energy conservation. Consequently, the response to infection is weaker in most forms of undernutrition. It is thus important to assume that the infection is present and treat the patient with broad spectrum antibiotics. Common infections in SAM include ear infection, urinary tract infection and pneumonia (WHO, 2000). Inability to control body temperature is also common during reductive adaptation. The child cannot produce heat and consequently is prone to hypothermia, a condition which often co-exists with hypoglycaemia and untreated infection (WHO, 1999).

Reductive adaptation is known to result in slow haemoglobin synthesis and as such iron that is not used for the making of haemoglobin is put into storage resulting in extra iron stored in the body (Cavalcante et al., 1998). It is recommended that Iron should not be given early during treatment as free iron can result in the formation of free radicals, bacterial growth and the formation of ferritin, a mechanism which uses the little energy and amino acids available for the body system (WHO, 1999).

Reductive adaptation is also associated with impaired electrolyte balance. During reductive adaptation, the potassium/sodium pump is less efficient and this causes low intracellular and high extracellular potassium and magnesium (WHO, 2000). Consequently, potassium is excreted in the urine causing overall body deficit. Potassium should therefore be given to make up for what is lost.

All in all, the impaired cellular machinery, the tissue deficits and abnormal body compositions have to be safely corrected to minimize death. Hypothermia, hypoglycaemia, and silent infections have to be managed first, and then multiple

specific deficiencies also have to be remedied. After the cellular machinery has been adequately repaired, the tissue deficits and abnormal body compositions can then be corrected as well (WHO, 2000).

2.4.2. The WHO "10 steps" as the standard protocol for treatment of SAM

The WHO 10-step guidelines for management of severe malnutrition (WHO, 1999) were developed based on a large body of research and clinical experience accumulated over 30 years (Heikens, 2007). Such research and experience include nutrition rehabilitation programmes in some health care centres in Uganda (Hay, Whitehead, 1973), research work in South Africa (Pretorius et al., 1956) and the Caribbean (Picou et al., 1978; Garrow, Picou, Waterlow, 1962) and several other areas around the developing world. These guidelines have been in existence since the early 80s (WHO, 1981) and have since undergone a series of improvements (WHO, 1999) including the most recent update of certain aspects of the 1999 guidelines which was published in 2013 (WHO, 2013).

The refinement of the WHO "10 steps" guidelines has largely been guided by emerging evidence from clinical and research practice (Ahmed et al., 1999). However, scientific investigation into mortality risk for SAM started way before the 80s. Prior to this period, there were debates on where and how to treat severely malnourished children (Jelliffe, 1970; Cook, 1971). Some of the first clinical risk factors thought to exacerbate mortality rates among severely malnourished children included electrolyte imbalance (Garrow, Smith, Ward, 1968), hepatic dysfunction, a variety of infections and anthropometric status (Gomez at al., 2000).

The WHO "10 steps" guidelines for management of SAM published in 1999 are currently promoted worldwide as the standard by which severely malnourished children should be treated (Schub, 2010). With strict adherence to these guidelines, mortality can be reduced to less than 5% (Ashworth et al., 2003). The guidelines include the initial *stabilisation phase* in which acute life-threatening problems such as hypoglycaemia and hypothermia are identified and treated and at which point cautious feeding is introduced. This is then followed by a longer *rehabilitation phase* which is a staged introduction of milk-based nutritional rehabilitation, micronutrient and vitamin supplementation, and the use of antimicrobial and anthelminthic treatment (WHO, 1999). Sensory stimulation, micronutrient supplementation and the correction of electrolyte imbalances are however initiated across both phases. Box 1 below illustrates the conventional WHO 10 step guidelines which were used for the management of SAM as part of this study (1999).

Step	Prevention	Warning signs	Immediate Action
1.Hypoglycaemia (Low blood glucose level) Hypoglycaemia is a blood sugar <3 mmol/l	1. Feed all children every 3 hours day and night. Start straightaway. 2. Encourage mothers to stay with very ill children to watch for any deterioration, help feed and keep warm.	1. Low temperature (hypothermia) noted on routine check. 2. Feels cold 3. Becomes drowsy or lethargic.	Dextrostix test on admission, before giving glucose or feeding. **If conscious and blood sugar is below 3mmol/l (or below 54mg/dl), or dextrostix are not available, or test cannot be done immediately:** 1. Give 10% glucose (50ml) or sugar solution (1 rounded teaspoon sugar in 50ml or 3½ tablespoons of water). 10% glucose is best, but give sugar solution or starter formula rather than wait for glucose. Test again 30 minutes after treatment. If blood sugar is still low, repeat 50ml 10% glucose or sucrose solution. 2. Feed starter formula every three hours (8 feeds), day and night. Start straightaway. (Use feed chart to find amount to give). **If unconscious, give glucose IV (5ml/kg of sterile 10% glucose solution).**
2. Hypothermia (Low temperature) Hypothermia is a rectal temperature below 35.5 ^{0}C or below 95.9 ^{0}F, or an underarm temperature below 350C or below 950F.	For all children:- 1. Feed straightaway and then every three hours, day and night. 2. Keep warm. Cover with a blanket, especially at night. Mother can keep child warm by sleeping in same bed. 3. Keep room warm, no draughts. 4. Keep bedding/clothes dry. Dry the child carefully after bathing (do not bathe if very ill). 5. Avoid exposure during examinations, after bathing.	Cold extremities, inactive, poor feeding NB. In malnourished children, hypothermia may indicate coexisting hypoglycaemia and presence of infection (see 5 below).	Take rectal temperature on admission (Ensure thermometer is well shaken down). **If the rectal temperature is below 35.5 ^{0}C:** 1. Feed straightaway (or start rehydration if needed). 2. Re-warm. Either put the child on the mother's bare chest (skin to skin contact) and cover them, OR clothe the child including the head, cover with a warmed blanket and place a heater or lamp nearby. 3. Feed every three hours (8 feeds). **Monitor during re-warming** • Take rectal temperature every two hours until it rises above 36.5 ^{0}C • Take every 30 minutes if heater is used because the child may become overheated
3. Dehydration (too little fluid in the body)	When a child has watery diarrhoea feed straightaway and give ORS* between feeds to	Profuse watery diarrhoea, sunken eyes, absent tears, dry mouth, slow skin pinch, sunken fontanelle,	**DO NOT GIVE IV FLUIDS EXCEPT IN SHOCK (see separate protocol for treating shock)** **If dehydrated:** 1. Give ORS 5ml/kg every 30 minutes for 2 hours (orally or by nasogastric tube), then 10ml/kg

	replace stool losses. As a guide, give 50-100ml after each watery stool for children <2 years and 100-200ml for older children. Continue feeding, including breastfeeding.	very thirsty, reduced amount of urine passed.	every hour for the next 4-10 hours. 2. Replace ORS at 4 hours, 7 hours and 10 hours with an equal amount of starter formula if rehydration is still in progress at these times. **Monitor during rehydration for signs of overhydration:** • increasing pulse and respiratory rate • increasing oedema and puffy eyelids (check for signs at least hourly)
4. Electrolyte imbalance (Too little potassium and magnesium, and too much sodium)	Limit the amount of salt in the diet		Give extra potassium and magnesium daily. **For potassium:** give potassium chloride solution orally: 250mg 3 times a day if <10kg, and 500mg 3 times a day if >10kg. If unavailable, give crushed Slow K ½ tablet/kg body weight daily. **For magnesium:** give Eastern Cape mineral/trace element mix: 2.5ml if <10kg, and 5ml if >10kg, daily. If unavailable, give 1ml of 2% magnesium sulphate daily, mixed with food
5. Infections	1.Good nursing care 2. Reduce overcrowding if possible. 3. Wash hands after dealing with any child and before examining the next. 4. Give measles vaccine to unimmunized children over 6 months of age.	NB The usual signs of infection, such as fever, are often absent so **assume** all severely malnourished children have infection and **treat with antibiotics.** Hypothermia and hypoglycaemia are signs of severe infection.	**Starting on the first day, give broad-spectrum antibiotics to all children.** **1. If the child has no complications, give Co-trimoxazole and Metronidazole** • Co-trimoxazole 5 ml paediatric suspension orally twice a day for 5 days (2.5ml if <4kg) • Metronidazole 7.5mg/kg 8-hourly orally for 5 days OR **2. If the child is severely ill** (apathetic, lethargic) **or has complications**(hypoglycaemia, hypothermia, raw skin/fissures, respiratory tract or urinary tract infection) give Ampicillin, Gentamicin and Metronidazole • Ampicillin 50mg/kg IM/IV 6-hourly for 2 days, then oral amoxycillin 15mg/kg, 8-hourly for 5 days or if amoxycillin is not available continue with ampicillin but give orally, 50mg/kg 6-hourly • Gentamicin 7.5mg/kg IM/IV once daily for 7 days • Metronidazole 7.5mg/kg 8-hourly orally for 7 days **3. If child fails to improve after 48 hours**, add Chloramphenicol 25mg/kg 8-hourly IM/IV for 5 days For parasitic worms, give mebendazole 100mg orally twice a day for three days

Step	**Management**
6. Micronutrient	1. Give Vitamin A on day 1. If under 6 months give 1capsule (50,000iu); if 6-12 months give 2 capsules (100,000iu); and if >12 months give 4 capsules (200,000iu). If the child has any signs of vitamin A deficiency, repeat this dose on day 2 and day 14.

deficiencies	Give the following daily: 2. Folic acid 2.5mg/day 3. Multivitamin syrup 5 ml daily 4. Zinc and copper. These are included in the Eastern Cape mineral and trace element mix along with magnesium (see 4 above). 5. Start iron (3mg/kg/day) as ferrous sulphate 5ml/day when you change to the catch-up formula. **(DO NOT GIVE IRON IN THE STABILISATION PHASE)**
7. Cautious feeding (stabilisation phase)	1. Give starter formula (see feed chart for amounts). These provide 130ml/kg/day. 2. Give 8 feeds over 24 hours 3. If the child has gross oedema, reduce the volume to 100 ml/kg/day (see feed chart for amounts) 4. If the child has poor appetite, coax and encourage the child to finish the feed. If unfinished, keep the leftovers and re-offer later. If eating 80% or less of the amount offered, use a nasogastric tube. If in doubt, see feed chart for intakes below which tube feeding is needed 5. Transfer to the catch-up formula as soon as appetite has returned (usually within one week) 6. If the child is breastfed, encourage continued breastfeeding but give starter formula first. For young children who are not breastfed, re-establish breastfeeding if possible. 7. Weigh daily and plot weight
8. Catch-up growth (rehabilitation phase)	1. Change to catch-up formula: - for 2 days, replace starter formula with the same amount of catch-up formula - on the next day increase each feed by 10ml until some feed remains uneaten 2. Give 7 feeds over 24 hours. These can be 7 feeds of catch-up formula, or 4 feeds of catch-up formula and 3 specially modified family meals of high energy and nutrient concentration 3. Actively encourage the child to eat as much as possible, so s/he can gain weight rapidly. Always offer more. 4. Weigh daily and plot weight
9. Loving care, play and stimulation.	1. Provide tender loving care. 2. Help and encourage mothers to comfort, feed, and play with their children 3. Give structured play when the child is well enough.
10. Preparation for follow-up after discharge	1. Obtain information on family background and socio-economic status. 2. Instruct mothers how to modify family foods, how often to feed and how much to give. 3. Send a referral letter to the clinic through i) clinic supervisor and ii) the mother. 4. Establish a link with community health workers for home follow-up. 5. Write full clinical summary in patient-held card.

Box 1: *Protocol for in-patient management of SAM for the Eastern Cape Province.*

2.5. Overview of the implementation of the WHO "10 steps" is South Africa

The WHO '10 step" guidelines have been shown to be feasible and sustainable even in small district hospitals with limited resources (Ashworth, 2004 & Deen, 2003). In their study on why some facilities perform better than others in the management of SAM, Cuming et al.(2007) showed that the implementation of the guidelines can be successful depending on the quality of care and sufficient training of nurses and medical staff. In some facilities, factors that interfere with effective delivery of optimal care include resource constraints (e.g. electrolyte/mineral mix), inadequate professional training, lack of commitment, and poor health system infrastructure (Puoane et al., 2004). Karaolis et al. (2007) also demonstrated that the sustainability of the guidelines was affected by insufficient staff knowledge and inattentiveness and argue that regular training is a key determinant.

Centres that have changed their treatment practices, however, have drastically reduced their case fatality rates (Puoane et al., 2004). Hlabisa hospital in KwaZulu-Natal for example reduced its case fatality from 20 % to 6% after improving the quality of care (Puoane et al., 2004). However, the sustainability of this significant drop in case fatality rate was not examined. In the Eastern Cape, the implementation of the WHO guidelines included training of paediatric staff, monitoring of the implementation of the guidelines as well as support and advocacy for sustained changes in management practices (Ashworth et al., 2003). This resulted in improved policies, quality of care and management systems, in two district hospitals, and subsequently in a further nine district hospitals within the poorest region of the Eastern Cape (Puoane et al., 2004).

2.6. HIV/AIDS and the burden of severe malnutrition

HIV/AIDS which is staggeringly affecting sub-Saharan Africa has changed the face of childhood malnutrition in terms of treatment and prevalence. In Sub-Saharan Africa, HIV infection has become more prevalent among children with SAM (Bachou et al., 2000; Kessler et al., 2000 & Ndekha et al., 2004). Evidence on the potential impact of HIV infection on survival of children with SAM has also begun to emerge. Some prevalence studies conducted in Africa have shown that severely malnourished children with HIV infection are more at risk of dying compared to their HIV uninfected counterparts (Chinkhumba et al., 2008; Ticklay et al., 1997; Prazuck et al., 1993; Mgone et al., 1991; Maayer and Saloojee, 2011)) especially if they are marasmic (Prazuck et al., 1993; Kessler et al., 2000). In some cases of severe malnutrition, HIV is co-morbid with tuberculosis. According to Heikens (2007), these co-morbidities have led to an epidemic of *secondary* severe malnutrition which is more associated with poor outcomes than *primary* severe malnutrition due to food shortage and non-HIV/TB related infections. Nevertheless, very few studies have assessed the differences in case fatality rates among HIV infected and uninfected undernourished children in the context of the recommended WHO treatment modality for SAM.

2.7 HIV infection in SAM and clinical response to the WHO therapeutic guidelines

A report compiled by the WHO working group (WHO, 2004) in which literature from 1998-2004 was reviewed confirmed an existence of knowledge gaps in relation to caring for severely malnourished children living with HIV/AIDS. This was also

confirmed in the recent WHO update of the 1999 ten-step guidelines which was compiled by nutrition task force (WHO, 2013). In both reports, there was recognition of the need for more rigorous studies to fill the knowledge gaps and achieve a clearer understanding of optimal case management of HIV infected severely malnourished children.

There is to date little evidence to show whether or not severely malnourished children who are infected with HIV differ from their HIV infected counterparts in their pathophysiological and clinical response to the WHO therapeutic guidelines for management of severe malnutrition. The information gap is particularly wide in relation to nutritional recovery, survival and growth rate between the two groups (Fergusson, 2009). The little evidence available has been inconsistent and reported findings generated from non-experimental studies which were conducted in different settings using a variety of treatment modalities or the modified WHO 10-step-guidelines (WHO, 2013). However, there have been few exceptions regarding case fatality rates. Most studies, however few, have constantly reported case fatality rates to be higher among HIV infected children, though to varying degrees (WHO, 2004).

Nutritional recovery is another important treatment outcome of SAM which has not been sufficiently explored. Evidence around this outcome also remains inconsistent. This is partly because of differences in study designs used to assess this outcome and the variety of therapeutic approaches used to address nutritional deficiencies of the study subjects. For example some studies in resource-poor Sub-Saharan countries have shown that although HIV positive severely malnourished children can achieve

normal nutritional status when given specific treatment protocols, the recovery is slower compared to HIV negative children (Ticklay et al., 1997, Ndekha et al., 2004; Sandinge et al., 2004). Fergusson et al, on the other hand, reported similar nutritional recovery (mean 8.9 vs 8.0 g/kg/day) among HIV infected and HIV uninfected severely malnourished children who survived.

In the most recent study, and possibly the only one conducted so far in South Africa, De Maayer and Saloojee (2011) investigated the clinical outcomes of severe malnutrition in the context of high tuberculosis and HIV co-infection. The study showed that severely malnourished HIV-positive children were five times more likely to die compared to HIV negative children despite good clinical care and access to highly active antiretroviral therapy. They also argue that SAM treatment guidelines need to emphasize the diagnosis and management of tuberculosis and HIV infection in endemic areas.

Although the authors did report that subjects received good clinical care, this claim may be considered as subjective as there was no mention of how the quality of care was evaluated in their study. Consequently, the effectiveness of the WHO treatment protocol for the management of severe malnutrition in the context of HIV infection may not be justifiably inferred from this study. An operational study incorporating the elements of epidemiology, care and outcome evaluation is therefore important in South Africa to substantiate the findings reported by De Maayer and Saloojee.

Further, there remains a paucity of studies in the literature which have investigated the relationship between the duration of hospitalisation and the rate of weight gain

achievable by children with and without HIV infection who survive while on treatment using the WHO treatment guidelines. There are only a few studies which have looked at the relationship between the nutritional status and the duration of stay in the hospital (Robinson, Goldstein and Levine GM, 1987; Messner et al., 1991 & Chima et al., 1997) but none of these estimated the number of days it took for cases to attain a certain rate of weight gain.

The sustainability of facility-based interventions which involve the implementation of the WHO treatment modality has also not been rigorously studied in resource-poor settings, including areas in South Africa. There are no studies which have "rigorously" examined whether gains realised in reducing CFRs and other important clinical outcomes related to SAM can be maintained and sustained in the facilities over time following the discontinuation of facility-based interventions. Some studies which examined the sustainability of such interventions used relatively less rigorous study designs (Ashworth et al., 2004; Schofield, Ashworth, 1996; Karaolis et al, 2007) with little or no consideration of the potential confounders of the observed trends in outcomes.

2.8. Theoretical and conceptual frameworks

This study was guided by three theoretical paradigms, namely: 1) The *normative theory*, 2) the *causative theory* (both of which constitute *the theory-driven enquiry approach*) and 3) *Gould's theory* of operations research.

2.8.1. Normative and Causative Theories in Theory-driven Enquiry

Theory-driven enquiry is premised on the view that health interventions often take place in settings or health care systems that are complex (Marchal et al., 2010). The complexity of such systems is often not detected by the traditional research designs which test the effectiveness of the intervention but do not take into account the underlying processes of change and the context of conditions that are needed to achieve the desired outcomes (Glouberman, Zimmerman, 2002).

This theory-driven approach was first developed in the 1980s for application in the field of social sciences with a view to making programme evaluation more comprehensive (Chan, Rossi, 1987). The approach adds an important element - *the programme theory of change* - to traditional approaches of programme evaluation which often use before and after and input output designs, or focus narrowly on methodological issues such as experimental and quasi-experimental design (Glouberman, Zimmerman, 2002).

According to Rossi et al. (2004), a programme theory of change depicts the programme's plan of operations, the logic that connects its activities to the intended outcomes, and the rationale for doing what it does. It allows the articulation of the programme in such a way that it is clear on how the programme is supposed to work, taking into account both the implicit and explicit assumptions underlying the programme at issue (Chen , 1990).

More often than not, if the goals and objectives of the programme being evaluated do not logically tie in with the conditions which the programme has been designed

to address, or the assumptions and expectations in the programme do not constitute a credible approach to attaining the desired outcome(s), it is highly improbable that the programme will be effective (Rossi et al., 2004).

Chen and Rossi (1987), proposed two components of the programme theory of change namely: the *normative theory* and *the causative theory* (Glouberman, Zimmerman, 2002). According to Marchal et al. (2010), the *normative theory*, also known as the *action model*, is an important tool that can be used to describe how the actual intervention was different (or not) from the planned intervention as well as the way the intervention was actually implemented (implementation fidelity). It also allows the evaluator to contrast the actual and intended outcomes of the intervention and ask whether these outcomes were a result of the intervention theory failure or the implementation failure.

The *causative theory* (causal model), on the other hand, allows the evaluator to tap into the mechanisms that lead to specific outcomes, particularly in terms of the relationship between the intervention and the outcomes, the potential influence of the intervention context as well as the moderating factors (Marchal et al., 2010). Figures 4 and 5 which were adapted from Marchal et al. (2010) illustrate the different components of the normative and causal theories, respectively.

The application of theory-driven enquiry in health systems research continues to gain momentum on a global scale (Marchal et al., 2010). This approach complements a number of traditional theories which have been in use for years within the realm of public health research, such as the Donabedian classical theory on quality of care

assessment (Donabedian, 1988) and Gould's theory of Operations Research (OR) (Gould, 2006).

2.8.2. Gould's theory of operations research

According to Gould (2006), the goal of OR is to optimize health outcomes through appropriate diagnosis, prescription and treatment. It is as such also referred to as "health outcomes research". Gould (2006) further argues that OR in public health is aimed at understanding the antecedent of the outcome by using analytic approaches developed by *epidemiology* and *quality of care research* to 1) characterize social and clinical factors as well as their resultant co-morbidities that create the specific risk, 2) determine the critical factors that shape the ways in which the practitioners perceive need, and then select and conduct a medical procedure to address it, and 3) compare the observed result to an "ideal" outcome that has been demonstrated to be possible in similar patients. A detailed explanation and a conceptual model of OR are provided in Chapter 4.

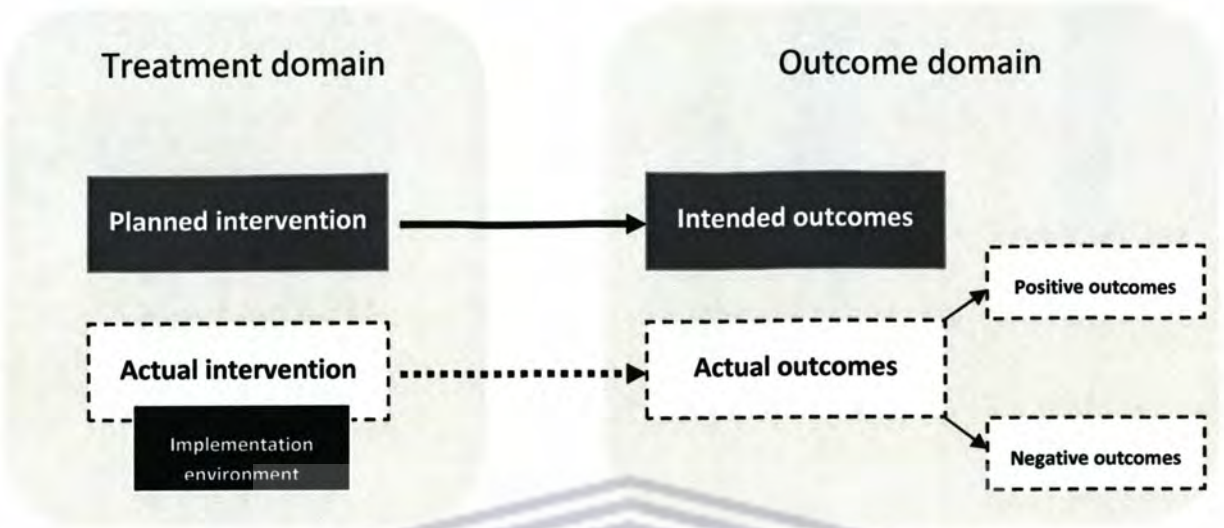


Figure 4: *Key elements of the Normative Theory*

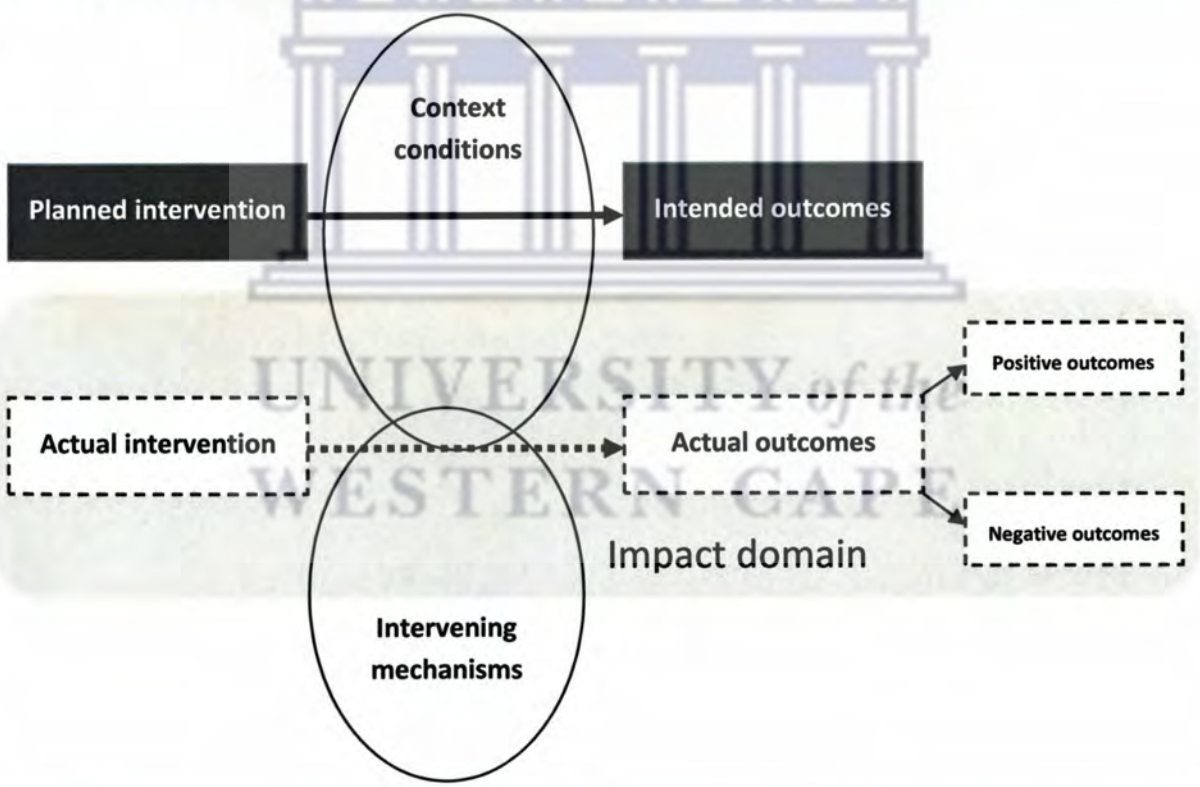


Figure 5: *Key elements of the Causative Theory*

2.8.3. Application of the three theories in the current study

Each of the three theories described above was applied during a particular phase of the study. The research phases (Phases 2, 3 and 4) which involved both quantitative

and qualitative methods was largely framed based on *Gould's theory of OR*. A conceptual framework of the OR is shown in Figure 6 in Chapter 4.

The *Causative theory* was used during Phase 1 to frame the study intervention and articulate how it is supposed to work. The specific causative theory for the study intervention showing the inputs and processes of care as well as the treatment outcomes in the context of the management of severely malnourished children with and without HIV infection is outlined in Figure 9 in Chapter 3.

The principles of the causative theory were again applied during phase 4 of the study to assess the programme context and moderating/intervening factors. The discussion section of the study was guided by the *normative theory* to draw up a distinction between programme theory failure and programme implementation failure and provide the recommendations for improving future interventions.

Chapter 3 introduces Phase 1 of the study in which the study intervention was developed. This phase was initiated in 2009 with a view to review and improve a training intervention introduced in 1998 to build capacity among health care workers so that they can manage SAM more effectively using the WHO 10-step treatment guidelines.

CHAPTER 3

STUDY INTERVENTION

PHASE ONE

3.1. Original intervention

The original intervention was initially launched in 1998 in 11 hospitals (including St Patricks and Holy Cross hospitals) in the Eastern Cape Province. The goal of this intervention was to reduce deaths from SAM and improve recovery using the WHO treatment guidelines. This 5-day training intervention was developed by the University of the Western Cape and the London School of Hygiene and Tropical Medicine with support from the Eastern Cape Department of Health. The initial structure of the training intervention and mode of delivery are described in Box 2 below.

1. **Group work,**	*To provide an opportunity for self-learning through logical reasoning and resolving problems, and promote deep learning that will not be forgotten*
2. **Role-plays**	*To facilitate discussions and raise sensitive issues, and to illustrate physiological mechanisms and difficult concepts in a memorable and light-hearted way*
3. **Practical exercises**	*To test knowledge and practise new skills*
4. **Questions and answers**	*To draw forth knowledge and apply this to managing malnourished children*
5. **Key messages**	*As a summary of the principles for managing severely malnourished children*
6. **Action plans**	*To help participants plan how they will improve their practices on returning to their hospitals*

Box 2: *Adapted from Puoane et al. (2006).*

Few years following the implementation of this training programme, a number of nurses who had received the training had either been transferred to a different ward

in the same facility, or left the hospital. This observation was made through follow-up visits to the facilities over a number of years post the intervention period. The peregrine nature of the health care workforce left a significant gap in the number of trained nurses who were able to treat the children admitted with SAM using the WHO guidelines. This meant that new nurses, without prior formal training on the use of the WHO guidelines, had to be deployed to the paediatric ward to replace those who had left.

The observations made during the site visits also revealed that there were some influxes of international medical doctors on short-term appointments who did not have the same training but were treating SAM cases. Furthermore, the health information system at ward level did not conform to the monitoring and evaluation standards. There were gaps in the quality of patient treatment records in terms of data accuracy, accessibility, reliability, timeliness, comprehensiveness, precision and confidentiality.

This called for a much more comprehensive intervention to ensure that there was continuity in the standards of patient care using the WHO guidelines in order to optimise outcomes. It was also important to ensure that the outcomes and processes of care could be more accurately and timely measured for OR purposes. Therefore, the original intervention was reinforced with additional literature-drawn components to make it an ongoing and multifaceted programme.

3.2. Revised intervention

The revised intervention and its additional components were implemented from January 2009 through to May 2013. For the sake of this study, only the period during which the revised intervention was active as per research specifications, is reported. These components were modelled on a similar intervention in Kenya which was implemented in 2008 as part of a cluster randomised trial to implement guidelines aimed at improving paediatric care in Kenyan hospitals (Ayieko et al. 2011). The aim of this intervention was also to reinforce the implementation of the best-practice guidelines and promote facility-level efforts to address organisational challenges. Generally, the revised intervention included the following components:

a. *Hospital visits conducted three monthly in each facility by the researcher to assess patient care and treatment outcomes using a standardised questionnaire (Appendix 9),*
b. *Six monthly feedback sessions presented by the researcher to the clinical and management staff in each hospital to report on findings based on the previous visit,*
c. *Regular induction sessions by the researcher with newly appointed nurses or nurses rotating in the paediatric ward to introduce them to the use of the guidelines and the study's information system,*
d. *Provision of job aides to facilitate patient care practices and documentation of treatment procedure. These included standardised dosage charts to use during the administration of antibiotics, multivitamins, electrolytes and ARV's as applicable (Appendix 10); fluid administration charts to record the amount of F75 and F100 given and left over (Appendix 11), An output chart to keep track of the patterns of diarrhoea, vomiting and urine discharge (Appendix 12); weight monitoring chart to monitor the rate of weight gain (Appendix 13); Four hourly temperature and pulse monitoring chart (Appendix*

14); as well as the Oral Rehydration Solution (ORSOL) chart to document the rehydration procedure followed during patient management (Appendix 15);

e. *Three monthly external supervision visits conducted by the research team over a period of two years to mimic the role of a clinic-based ward supervisor – in this case a senior nurse in the paediatric ward. This process involved observing nurses to ensure that they were correctly implementing the guidelines, guiding them in case of poor implementation of the guidelines, playing an interface role between front line health care workers and the hospital management and onsite problem solving.*

f. *Baseline identification of fulltime senior paediatric nurses based in the paediatric ward in each hospital. The paediatric nurses were responsible for owning and sustaining the intervention during and after the study period. They acted as mentors for junior nurses and newly appointed or rotating nurses. The mentors introduced these nurses to the utilisation of the intervention components over and above their routine duties such as solving on-site problems;*

g. *Six monthly meetings with the hospital management team to alert them to issues hampering optimal patient care.*

h. *Linkage with a facility-based social worker who initiated a follow-up process with community-based and government departments to ensure that SAM cases that get discharged receive adequate support to prevent relapses and readmissions to the hospital.*

These additional components are also summarised in Figure 9 as the darker shaded boxes embedded in the overall intervention theory of change. The assumptions underlying this theory as well as possible moderating variables are summarised in Table 1. Only assumptions that were critical to the effectiveness of the intervention were considered.

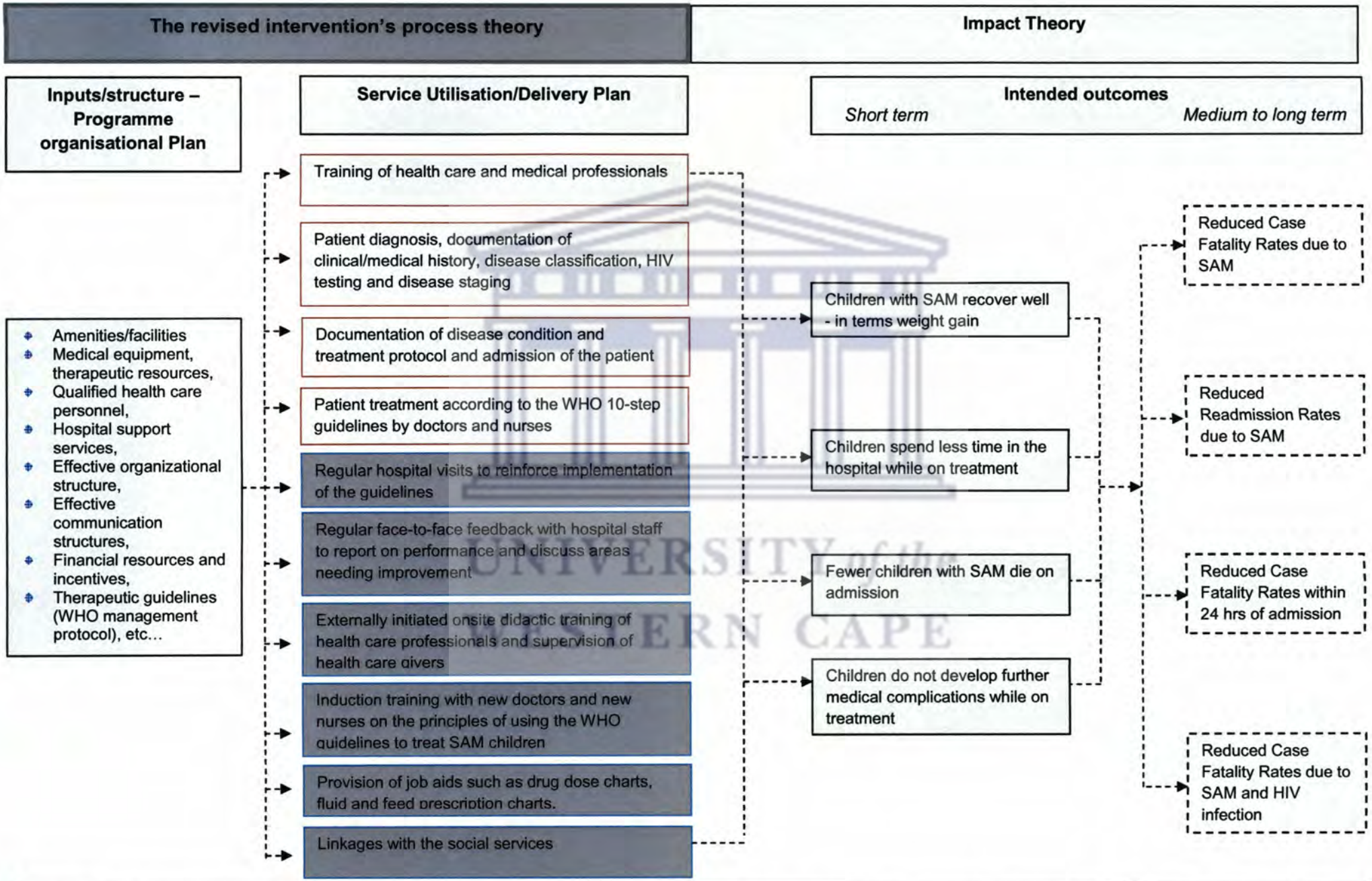


Figure 9: *A theoretical framework based on process, structural and outcome indicators of quality of care for severe malnutrition in the context of HIV infection.*

Table 1: *Assumptions underlying the intervention as well as possible moderating factors*

Factors presumed to affect the effectiveness of the intervention	The actual problem and what was done about it in the evaluation
Individual Level	
Nurse or Mentee background: Knowledge, experience, education	**Issue:** *Some frontline implementers of the intervention may not have the same level of background knowledge to absorb and make use of the new content they have been exposed to during the training or mentorship sessions.* **Solution:** *Data analyses involved longitudinal assessment of the outcomes of the intervention both within and between the two hospitals. This was done as part of the interrupted time series design whose ability to control for selection bias is comparable to that of the randomised controlled trials.*
Nurse/Mentee motivation to implement the intervention as specified:	**Issue:** *Some evaluators have advanced the view that participation in facility based implementation of health interventions is motivated more by factors other than the desire to do so.* **Solution:** *It is hoped that the time series design to assess longitudinal variations in the hospital performance metrics might have alleviated this issue. It is assumed that there was a fair distribution of motivated and less motivated hospital staff across various data points during the study period.*
Organization/Facility Level	
Management support: Staff access to management and/or mentoring; management belief in the programme, motivation to support programme implementers	**Issue:** *Training implementers report that management support for trainees to perform new skills is highly variable across facilities.* **Solution:** *Questions were included in follow-up interviews with the clinical teams in both hospitals about management support. This was done as part of the qualitative phase. It was assumed that the analysis of these qualitative results would tease out whether performance outcomes were affected by any management-related barriers to implementing the intervention. Both between and within facility analyses were*

	performed
Human resources: Staffing levels, burnout etc.	**Issue:** *Many facilities are understaffed. This results in high patient loads and burnout among staff. This could affect the ability of the nurses and mentees to implement the intervention as optimally as possible.* **Solution:** *Questions about staffing levels and burnout were included in the follow-up phase of this study.*
Supplies and equipment: Medicines, medical supplies, equipment	**Issue:** *Key medicines and other necessary supplies and equipment for optimal implementation and adoption of the intervention at facility level may not always be available.* **Solution:** *An observation component consisting of regular visits to the hospital was included in the study.*
Facility systems: Appointments, records, patient flow, referrals	**Issue**: *Records at most facilities are paper-based, and sometimes incomplete.* **Solution:** *Patient records were reviewed to determine whether or not reporting quality is sufficient, and where necessary data quality enhancement mechanisms were instituted and reinforced*
Health System/Population Level	
Policies (national, regional, local):	**Issue**: The scope *of practice for this particular intervention may not be clearly articulated in or supported by national policies and therefore adoption at facility level may be a challenge* **Solution:** *In the follow up interviews conducted during phase four of the study, questions about policy-related barriers to implementing the intervention were included.*
Available support structures: Laboratory services, procurement services referral systems	**Issue**: Effectiveness of the programme at patient level may be influenced by the presence or absence of support structures beyond the health worker-patient interface. **Solution**: *During the follow up phase of the study questions on the role of the support structures in facilitating the implementation of the programme were included.*

The actual theory of change underlying the revised intervention consists of the ***intervention's process theory*** as well as ***the impact theory***. The revised intervention process theory which is depicted in Figure 9 constitutes the Programme Organisational Plan and the Service Delivery/Utilisation Plan. The intervention's Service Utilisation/Delivery Plan posits the critical assumptions about how SAM cases that benefit from the revised intervention actually engaged with the intervention right from the beginning and followed through to the point of receiving sufficient exposure that may or may not bring about the desired changes shown in the Intervention's Impact theory. The intervention's Organisational Plan on the other hand shows the functions and activities that the revised intervention should have performed and the human, financial and physical resources that were required for that performance to be realised. The viability of the organisation plan also served as a tool to contextualise the effectiveness of the service delivery system and ultimately the ability of the intervention to produce the desired outcomes and impact.

As depicted in Figure 9, the intervention's Impact Theory of Change shows the hypothetical pathways linking the programme delivery and organisational plan to some intermediate conditions that are assumed to improve the programme outcomes and impact. The impact theory attempts to highlight the dependence of the more distal, and generally more important, outcomes that demonstrate impact on successful attainment of the more proximal ones. For example, the reduction of readmission rates due to SAM was dependant, in part, on improvement in the rate of weight gain and prevention of medical complications while on treatment, amongst

other short term outcome. As such, outcome and impact monitoring and evaluation were done in that order, starting from the short term, to medium term outcomes and ultimately long term outcomes/impact of the intervention.

3.3. The candidate's contributions to the entire study

This was a long-standing study which began in 1985 as explained earlier section 3.1. Based on the original design of the study, the candidate was able to develop a different research angle (as shown under the aims and objectives) around which he *independently* achieved the following:

1. Conducting the literature review and identifying gaps from previous related research
2. Developing study designs to answer the research questions at issue
3. Revising the original intervention using evidence-based approach
4. Strengthening and monitoring implementation (process monitoring) of the revised intervention as described in section 3.2 under point a) through to h)
5. Developing data collection tools for programme process and outcome monitoring and evaluation
6. Carrying out data collection on a regular basis
7. Capturing all the data collected over the study period
8. Conducting statistical and qualitative data analyses for the entire study but ensuring that consultation is carried out with senior biostatisticians for verification of results and interpretation thereof
9. Presentation, interpretation and discussion of the results

CHAPTER 4

STUDY METHODOLOGY

4. 1. Introduction

This chapter firstly introduces the aims, objectives and hypotheses of the study and then outlines all the methodologies used to conduct the study.

The research phase of the study involved three successive phases. The methodological section is therefore organised in the order in which the study was conducted. For each research phase, a comprehensive account of the study design, data collection tools and methods as well as data analyses techniques used are discussed.

Phase 2 of the study started just after Phase 1 was completed. The second phase was aimed at modelling crude and adjusted effects of HIV infection, disease stage and other comorbidities, as well as the quality of care on the survival prospects of SAM cases with and without HIV infection following the intervention. Phase 2 also involved an assessment of the relationship between duration of hospitalisation and the rate of weight gain among the same study subjects.

Phase 3 of the study was initiated in 2013 to estimate the impact of discontinuing the revised intervention on selected system-level outcomes related to SAM in the study setting. The empirical findings obtained from Phases 2 and 3 were used to guide the development of Phase 4. This phase was initiated in 2014 and involved the use of qualitative methods in the form of Focus Group Discussions with facility-based personnel. For the sake of reporting, the observational aspect of the study was combined with Phase 4. All the three research phases were conducted within an Operations Research framework with a Sequential Explanatory Mixed Methods

Design. Before a full account of the mixed methods approach and the individual study designs are given, the concept of OR and its origin and application in public health research are first explained.

4.2. Study aim and objectives

4.2.1. Aim

To develop, implement and evaluation a facility-based structured intervention aimed at improving treatment outcomes of children admitted with Severe Acute Malnutrition and other comorbidity to two District Hospitals in the Eastern Cape Province in South Africa.

The study consisted of four phases each with an overall objective as shown below:

4.2.2. Objectives

PHASE ONE

Objective 1: To development of the study intervention

1. To review the implementation of the intervention originally developed to manage severely malnourished children admitted to two district hospitals in the Eastern Cape Province;
2. To refine tools that were used to measure cross-sectional and longitudinal performance of the two hospitals regarding the management of SAM;

PHASE TWO – PART ONE

Objective 2 (a): To develop a risk factor epidemiological model of SAM in the context of the WHO "10-step" guidelines

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3. To determine survival among children who were admitted with SAM and treated according to the WHO guidelines for management of SAM by HIV status, ;
4. To examine whether there were differences in survival among HIV positive severely malnourished children who were supposedly treated according to the WHO guidelines and were at different clinical stages of HIV infection;
5. To assess both the singular and interactive effects of other clinical manifestations on the survival of SAM cases, over and above HIV status and disease stage;
6. To assess the association between different syndromic manifestations of SAM, HIV status and the clinical stages of HIV infection;
7. To assess compliance to the WHO ten-step treatment guidelines in the two study hospitals;

PHASE TWO – PART TWO

Objective 2 (b): To assess the relationship between duration of hospitalisation, the rate of weight gain and HIV infection in the context of the WHO "10-steps'guidelines

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8. To assess the relationship between the rate of weight gain and a) SAM syndromic manifestations, b) HIV status and 3) HIV disease stage;
9. To determine whether these relationships differed by hospital;
10. To determine the relationship between duration of hospitalisation among cases who survived and a) SAM syndromic manifestations, b) HIV status and 3) HIV disease stage;
11. To estimate the number of days it took SAM cases with and without HIV infection to achieve different rates of weight gain;
12. To assess whether the relationship between the number of days spent in the hospital and rate of weight gain differed by hospital;

PHASE THREE

Objective 3: Sustainability assessment of the revised intervention

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13. To assess, in statistical terms and for each hospital, how much the discontinuation of the revised intervention changed the level and trend of selected outcome indicators which are related to the management of SAM, immediately and overtime;
14. To compare the temporal changes of the outcomes (Total mortality rate associated with SAM, SAM deaths within 24 hours of admission, Mortality attributable to SAM and HIV) between the two hospitals
15. To determine the sustainability of the revised intervention based on the findings from objective 15;

PHASE FOUR

Objective 4: Contextualisation and explanation of the quantitative findings

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16. Hospital To explore with each group some of the possible factors that may help explain the pattern of the quantitative results, in terms of:
    a. The structural and functional characteristics of the hospital milieu and
    b. The characteristics of the broader health care system;
17. To clarify with the hospital staff how these characteristics impacted their day to day application of the WHO treatment guidelines for management of SAM.

4.3. Study Hypotheses

PHASE TWO - PART ONE

Main hypotheses

1. The differences between the two hospitals in terms of the clinical profile of SAM cases on admission were not statistically significant
2. There was no statistically significant difference between HIV infected and uninfected SAM cases with regard to syndromic classification of SAM
3. There was no statistically significant difference in survival prospects of SAM cases between the two hospitals, if no other clinical characteristics were considered
4. If HIV status was considered, there was no statistically significant difference in survival prospects of HIV infected and uninfected SAM cases between the two hospitals
5. There were no statistically significant survival differences across the four HIV clinical stages among SAM cases who were HIV positive
6. Critically ill SAM cases were not statistically different from the non-critically ill cases in terms of survival, both within and between the two hospitals
7. Age, hospital, SAM syndromic classification, oedema grade, dermatosis grade, co infection with LRTIs, other comorbidities, being critically ill on admission, HIV disease stage and the quality of care received were not associated with mortality among SAM cases

8. Being critically ill on admission, having HIV co-infection and/or LRTIs comorbidity were not statistically significant effect modifiers of risk of death among SAM cases

PHASE TWO – PART TWO

Main hypotheses

9. There were no statistically significant differences ***between*** and ***within*** the two hospitals in terms of the relationships between HIV status and a) the rate of weight gain and b) the duration of hospitalisation among SAM cases.
10. There were no differences in the mean rates of weight gain between HIV infected and uninfected SAM cases at different time intervals

PHASE THREE

Main hypotheses

11. During the intervention period, there was no statistically significant month-to-month decrease in mortality associated with the three performance indicators (Total mortality rate associated with SAM, SAM deaths within 24 hours of admission, Mortality attributable to SAM and HIV) in both hospitals

12. There was no statistically significant trend increase in the three performance metrics related to SAM following the discontinuation of the revised intervention

13. The baseline level of mortality for all three indicators was not different from the end point (end of the study) level of mortality

4.4. Study setting

This study was conducted in two district hospitals namely St. Patrick's hospital in Bizana and Holy Cross hospital in Flagstaff. Both hospitals are situated in the Eastern Cape Province of South Africa (See Figure 1). The province is located in the former Transkei, an Apartheid-era homeland and one of the most under-resourced regions in South Africa (Puoane et al., 2006). These hospitals were selected based on the fact that they had participated in the initial training programme as part of a province-wide intervention to improve the management of SAM in the Eastern Cape Province (Ashworth et al., 2003). This was important because these hospitals had better infrastructure and systems in place to accommodate the implementation of the intervention. Other hospitals in the region were poorly resourced and not viable options for a resource intensive intervention that was not going to provide the resources at issue. They two hospitals were also identified as having been implementing the WHO 10-step guidelines better than the rest (Cumming et al, 2007).

According to the Municipal Demarcation Board (2008), St Patrick's hospital serves the Mbizana local municipality which, by the year 2008, had a population size of about 280000 people residing in close to 48000 households, and with a percentage

population growth of 12.1% from 2001 to 2007. Holy Cross hospital, on the other hand, serves Qaukeni local municipality and had an almost similar population size and number of households as Mbizana municipality in the same year. However, it had a much smaller percentage population growth of about 9% from 2001 to 2007.

In terms of HIV prevalence, the 2005 report from the European Consultants Organisation on the district profile of the Eastern Cape O.R. Tambo District Municipality indicated that HIV prevalence was at 29.2% in 2003 in the region as a whole. Some of the key developmental issues in the region which were identified by the local population in 2008 included poverty, unemployment, suboptimal health status and safety (Municipal Demarcation Board, 2008).

Throughout the study period, admissions related to SAM in both hospitals constituted on average 50% of the total ward admissions in the paediatric ward. At St Patrick's hospital, the paediatric ward had on most days one paediatric nurse, one senior nurse, two to three staff/student nurses and one medical officer. At St Holy Cross hospital on the other hand, there was one paediatric nurse, and three to four nurses plus a medical officer who would be rotating in the paediatric ward.

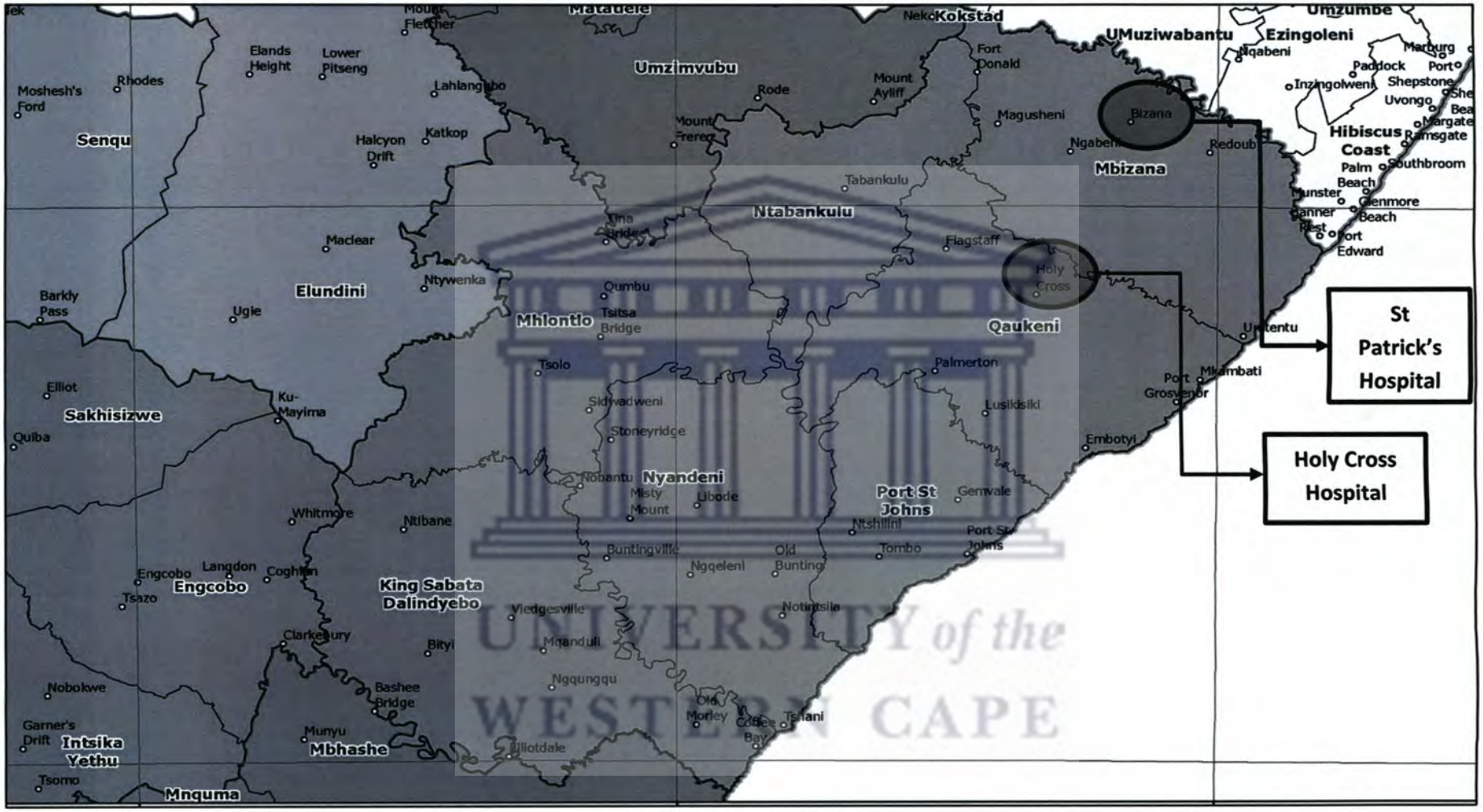

Figure 1: *Location of the two study sites in the Eastern Cape Province*

4.5. Operations Research Paradigm in the realm of public health research

The techniques of OR were originally developed and used in the 1940's to guide military operations, but were later adapted in the field of industrial management for decision making (Churchman *et al.* 1957). At the time, the application of OR in the field of public health was uncertain. Some scientists argued that, for many years to come, there would be little potential for the mathematical programming techniques used in OR for military and industrial purposes to be utilised directly in the field of public health (Andersen, 1964). However, few years later, OR techniques eventually began to be recognised within a number public health settings in the United States and the United Kingdom (Committee of Enquiry, 1956; Bailey, 1957) , and have since gained momentum across the globe.

There is currently a drive to move away from the exclusive use of mathematical models in OR to develop and apply other research methods that produce equally useful scientific evidence. A collaborative effort between the Global Fund to fight AIDS, Tuberculosis and Malaria; the Special Program for Research and Training in Tropical Diseases (TDR); and an inter-agency technical working group comprising representatives from the WHO, UNAIDS and USAID; have been at the fore front of this paradigm shift. The consortium developed a framework for operations and implementation research in health and disease control programmes which recognises OR as:

> "Any research producing practically-usable knowledge (evidence, findings, information, etc.) which can improve program

implementation (e.g., effectiveness, efficiency, quality, access, scale-up, sustainability) regardless of the type of research (design, methodology, approach)" (WHO, 2008:11)

The main purpose of Operations Research is thus to provide scientific evidence for health and disease control programmes to improve their quality as they scale up. Through the application of rigorous analytical methods, the decision makers of a particular programme are able to understand how their programmes work and to make evidence-based programme decisions by choosing between various courses of action available to improve programme quality (WHO, 2008).

Figure 6 below outlines the major Operations Research steps followed to conduct the three research phases. This diagrammatic representation was adapted from the WHO (2008). Each step shown in Figure 6 involved specific research activities which, together, constituted a MMD as explained in the next section of this chapter.

4.6. Mixed methods approach

4.6.1. Definition

Over the years, several definitions of Mixed Methods Designs have emerged, most of which focused on various elements of the methods, research processes, philosophy, and research design (Creswell and Clark, 2011). Early publication on Mixed Methods Designs have referred to them as those that include at least one quantitative method and one qualitative method, where neither type of method is linked to any specific inquiry (Greene, Caracelli, and Graham, 1989:256). Other writers have referred to

them as multi-method, integrated, hybrid, combined and mixed methodology research (Creswell and Plano Clark 2007: 6).

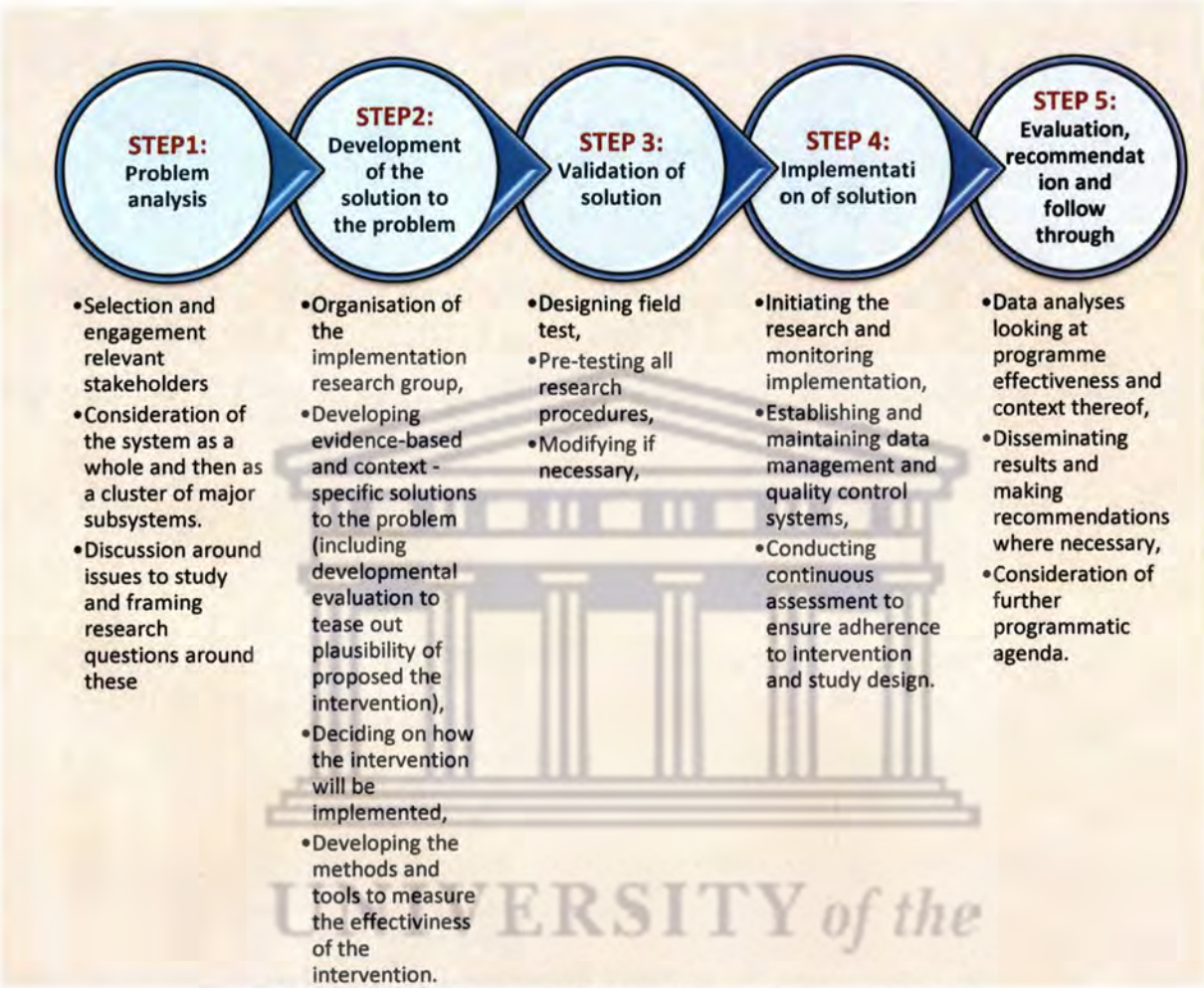

Figure 6: *A model for Operations Research in Public Health (Adapted from WHO, 2008)*

The reasoning behind mixing both kinds of methods within one study is that neither quantitative nor qualitative methods are sufficient, by themselves, to capture the trends and details of a situation. The mixed-methods designs therefore allow for the expansion of the scope or breadth of an enquiry so as to counterweight the weaknesses of either approach alone (Blake 1989; Rossman and Wilson 1991).

Johnson and colleagues combined diverse perspective on the MMD and came up with the following composite definition:

"Mixed methods research is the type of research in which a researcher or team of researchers combines elements of qualitative and quantitative research approaches (e.g., use of qualitative and quantitative viewpoints, data collection, analysis, inference techniques) for the broad purposes of breadth and depth of understanding and corroboration" (Johnson, Onwuegbuzie et al. 2007:123).

4.6.2. Some types of the mixed methods design

The MMD can be used for different purposes. Therefore, they may take different forms to suit a particular research agenda. Creswell et al. (2003) identified four major types of MMDs, namely: *The Triangulation Mixed Methods Design, The Embedded Mixed Methods Design, The Explanatory Mixed Methods Design and the Exploratory Mixed Methods Design*. According to Creswell and colleagues, the *triangulation Mixed Methods Design*, which is by far the most commonly used design in research, entails the concurrent but separate use of quantitative and qualitative methods during the same timeframe with both having equal weights. The *Embedded Mixed Methods Design*, on the other hand, involves mixing different datasets at the design level of the study, so that one dataset provides a supportive and secondary role in the study based on the other data type. The third type, the *Exploratory Mixed Methods Design*, has also been defined by Creswell et al. (2003) as a two phase design in which the results of the first method (usually qualitative) can help develop or inform the second phase (usually quantitative), particularly in situations whereby measures of a quantitative instrument are not available (e.g. new variables have to be generated) or there is no guiding framework or theory (Greene et al. 1989).

The *Explanatory Mixed Methods Design*, which is also known as a *"Sequential" Explanatory Mixed Methods Design*, has been described by Creswell et al. 2003) as consisting of two distinct phases: The quantitative phase followed by the qualitative phase. The investigator first collects and analyses the quantitative data, then the qualitative data are collected and analysed second in sequence to substantiate or help explain the quantitative results obtained in the first phase (Ivankova, Cresswell and Stick, 2006). Ideally, depending on the nature of the research, the quantitative phase provides a general understanding of the research problem whereas the qualitative phase refines and explains statistical results by way of an in-depth exploration (Tashakkori and Teddlie 1998).

According to Creswell et al. (2003), the sequential explanatory Mixed Methods Design comprises two variants: The *follow-up explanation model* and the *participant selection model*. The former focuses on the results to be examined in more detail and the later focuses on the appropriate participants to be selected.

During the current study, the ***follow-up explanation model*** as a variant of **the sequential explanatory Mixed Methods Design** was used. The process involved in collecting and analysing data for the two phases is described in Figure 7 below.

4.7.1. Phase 2

As all research subjects in phase 2 of the study were minors, permission for their participation was first sought from their parents or guardians using a written consent form which was written in either English (Appendices 1) or IsiXhosa (Appendices 2), a local language spoken and understood by most participants in the

study setting. The participant information sheets also written in English (Appendices 3) and IsiXhosa (Appendices 4) were read out to the parents/guardians to give them relevant information about the research. They were informed that they may refuse to have their children participate in the study or withdraw from the study at any time without fear of victimization from the research team or others. Parents/guardians were further informed of the use to which the research will be put, as well as of any other implications of the research.

During the management of patients, suboptimal patients care occurred, though on rare occasions from nurses, particularly those who had not yet received induction training for the management of SAM. It was the responsibility of the researcher to speak directly to the health care worker to rectify the mistake onsite or show them how to not repeat the mistake, the senior nurse and doctor would also be alerted to the recurrent mistakes that were being noted for them to provide more informed instructions to the nurses who are at the fore of patient care.

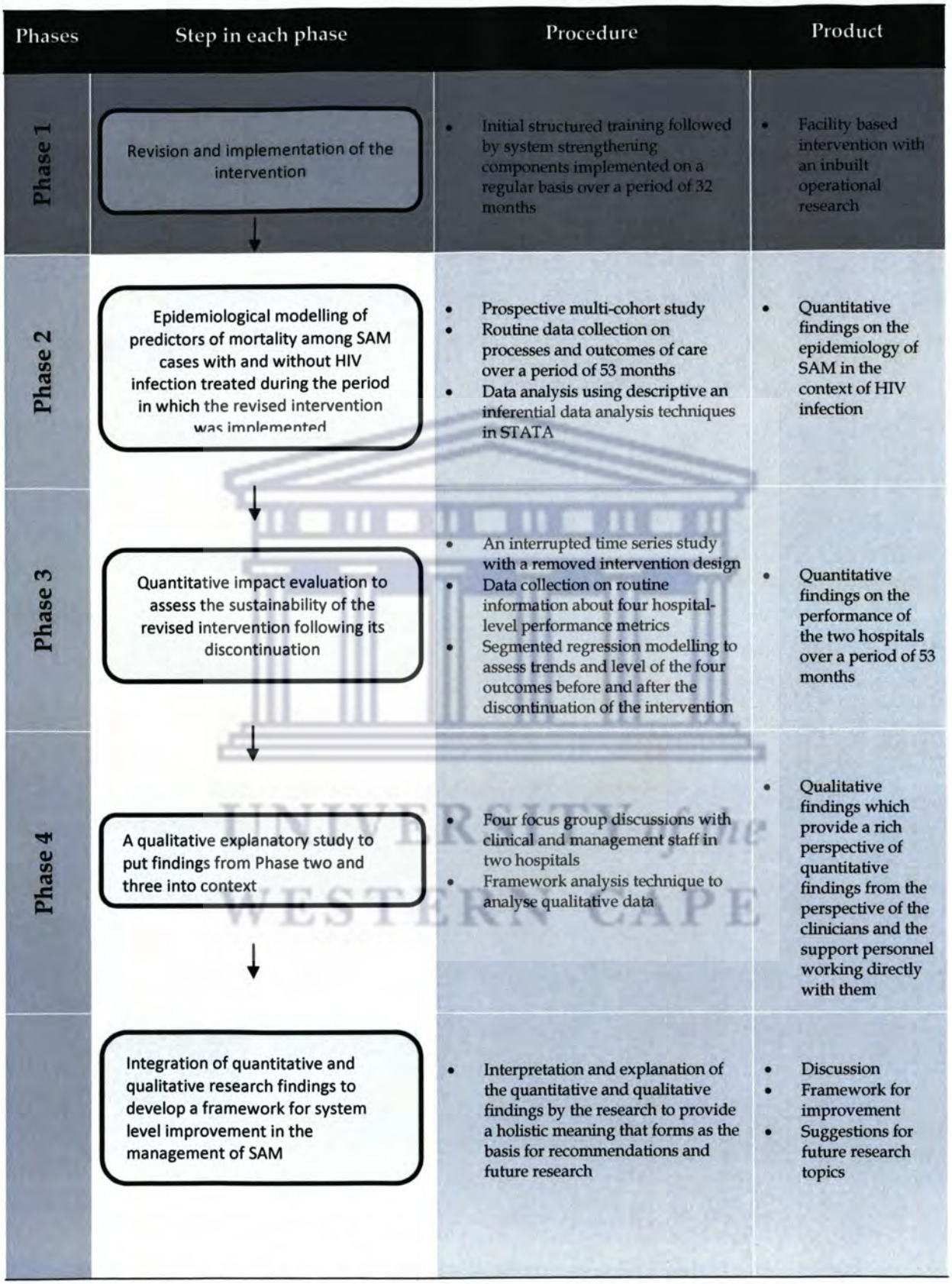

Figure 7: *An illustrative Model of the Sequential Explanatory Mixed-Methods Design Procedures for the study*

4. 7.2. Phase 3

Phase 3 of the study did not require consent from any participants. This phase involved collecting secondary data from the each hospital which required permission from the hospital management. The permission was granted as part of the overall study.

4. 7.3. Phase 4

The hospital personnel who participated in FGDs were informed that their confidentiality may not be ensured during the discussion as what they shared during the discussion was heard by people in the group. However, they were requested not to discuss the information shared with anyone else after the discussions were completed. Also, after the discussion the researchers played their part to ensure that information which participants had shared was not revealed to any other person other than the researchers. Participants who took part in FGDs received a separate participant information sheet (Appendices 5 and 6) describing the purpose and nature of the study prior to the commencement of the interviews. Interviews then began after a hand-signed consent form (Appendices 7 and 8) had been obtained.

All respondents in Phase 2 and 4 were informed that in the event of any difficulties arising from the research, they would be referred to the appropriate persons or organizations. Participants were also informed that no direct benefits and harm were to be anticipated from the study and that it was being conducted for academic purposes. Participation was voluntary, with no form of coercion used against them.

Permission was also sought to tape-record the interviews where applicable. After data collection, all the information collected was placed in a location with restricted access until analyses were completed. Information collected and the forms used to obtain consent will be stored for 6 years post data analyses for future reference should any ethical issues that require verification arise during this period.

PHASE TWO

4. 8. Risk factor epidemiological modelling of SAM in the context of the WHO "10-step" treatment guidelines

The methods section for Phase 2 of the study was organised based on the "*Strengthening the Reporting of Observational Studies in Epidemiology*" (STROBE) criteria (WHO, 2007). STROBE is an international collaborative initiative of epidemiologists, methodologists, statisticians, researchers and journal editors who are involved in the conduct and dissemination of observational studies. The primary aim of STROBE is to promote adequate reporting of research methods and results to allow for a more objective assessment of the strengths and weaknesses of observational studies (Von Elm et al., 2008).

4. 8.1. Study design

Phase 2 of the study involved a combination of an observational prospective study design as well as a retrospective component. The prospective aspect of the study involved identifying and classifying multiple cohorts of SAM cases admitted to two different hospitals at different study intervals with respect to their nutritional and

HIV status and following them over a period of time to assess specific treatment outcomes. Thadhani and Tonelli (2006) defined the term *cohort* as a group of individuals who have a common feature when they are assembled and who are followed in a specific time period. The common aspect of a prospective cohort study design is that it allows researchers to define temporal sequence between exposure and outcome thereby alleviating the risk of recall bias (Thadhani, Tonelli, 2006). The retrospective component involved reviewing treatment records which were compiled prospectively to document outcomes of interest as well as assess the quality of care.

4. 8.2. Study participants

Study cases were children admitted to both hospitals with SAM between January 2009 and May 2013. Cases were only eligible for recruitment in the study if they were between the ages of 6 months and 5 years, had patient treatment records with clearly defined malnutrition status (marasmus, kwashiorkor, marasmic-kwashiorkor), had records showing HIV test results and HIV clinical stage (for HIV positive cases) and had a complete treatment record while in the hospital. A comprehensive written medical examination by a doctor as well as the discharge criteria followed for cases that did not die while on treatment were also used as eligibility criteria. However, a few exceptions were made for cases that did not fulfil some inclusion criteria such as the lack of a fully written examination by the doctor and the lack of discharge criteria followed to discharge a case following treatment. The exclusion of a large number of cases from the study from the main pool would

have significantly affected the statistical tests used to analyse the data as well as the inferences thereof.

4. 8.2.1. Sample size calculation

The required sample size was calculated using Stata/IC 13.0 (Statacorp, 2013). Two Stata commands derived from the main statistical tests used during data analysis were used as follows:

For the log rank test, the sample size was calculated to achieve 80% power ($1-\beta = 0.8$) and detect 50% hazard of death in the HIV positive study group ($\Delta_a = 0.5$) at the end of the study. A two-sided $\alpha = 0.05$ and a 1:1 ratio for the number of cases in both the HIV positive and HIV negative study groups were considered. The accrual period (period during which subjects were being recruited into the study) was considered to be equal to zero as all cases were recruited and immediately put on treatment. However, the observation period (additional follow-up time after the end of recruitment during which cases were under observation) was set at a minimum of 60 days for each cohort of patients recruited into the programme during a specific month. It was also assumed that there would be no withdrawals from the study.

Based on these input parameters and assumptions, the *stpower logrank* command in STATA 13.0 estimated the number of events (E) to be 72, and the estimated sample sizes for the two-sample comparison of failure functions to be 180 cases (N), of which 90 were HIV negative cases (N1) and 90 HIV positive cases (N2).

For the two-sample comparison of exponential failure curves using the hazard ratio estimates, a uniform accrual and follow-up period were considered for both HIV

positive and HIV negative subgroups. The parameters specified were: α=0.05, study power (1-β = 0.9), and the difference between the hazard ratios $\delta = \lambda_2 - \lambda_1 = -0.55$, where λ_2 and λ_1 represent the hazard ratio in the HIV positive and HIV negative groups respectively, but holding other covariates constant. Stata default hypotheses (H_o: $\delta = 0$ vs H_a: $\delta \neq 0$) were used. The resultant sample size (N) generated by the *stpower exponential* command was 126, of which N2 and N1 were both equal to 63.

At the end of the study, a surplus of SAM cases had been recruited into the study. In total, about 450 SAM cases, 57% of which were HIV negative and 43% HIV positive, were included during data analysis.

4. 8.2.2. Participant recruitment procedure

The parents/guardians of severely malnourished cases were approached in the ward and firstly informed about the study. This was done following diagnosis and referral of SAM cases from the outpatient department where they were first seen by the Doctor. On the day of admission, parents/guardians were requested to provide consent so that their children could be screened for HIV infection. Mothers/Guardians who provided consent, had their children screened and based on these screening results, 2 broad groups were formed: group A (HIV negative cases) and group B (HIV positive cases). Group B was further divided into 4 categories based on the clinical stage of HIV infection as defined by the WHO guidelines for staging infants and children (WHO, 2005). Figure 10 illustrates the flow chart for the participant recruitment and screening.

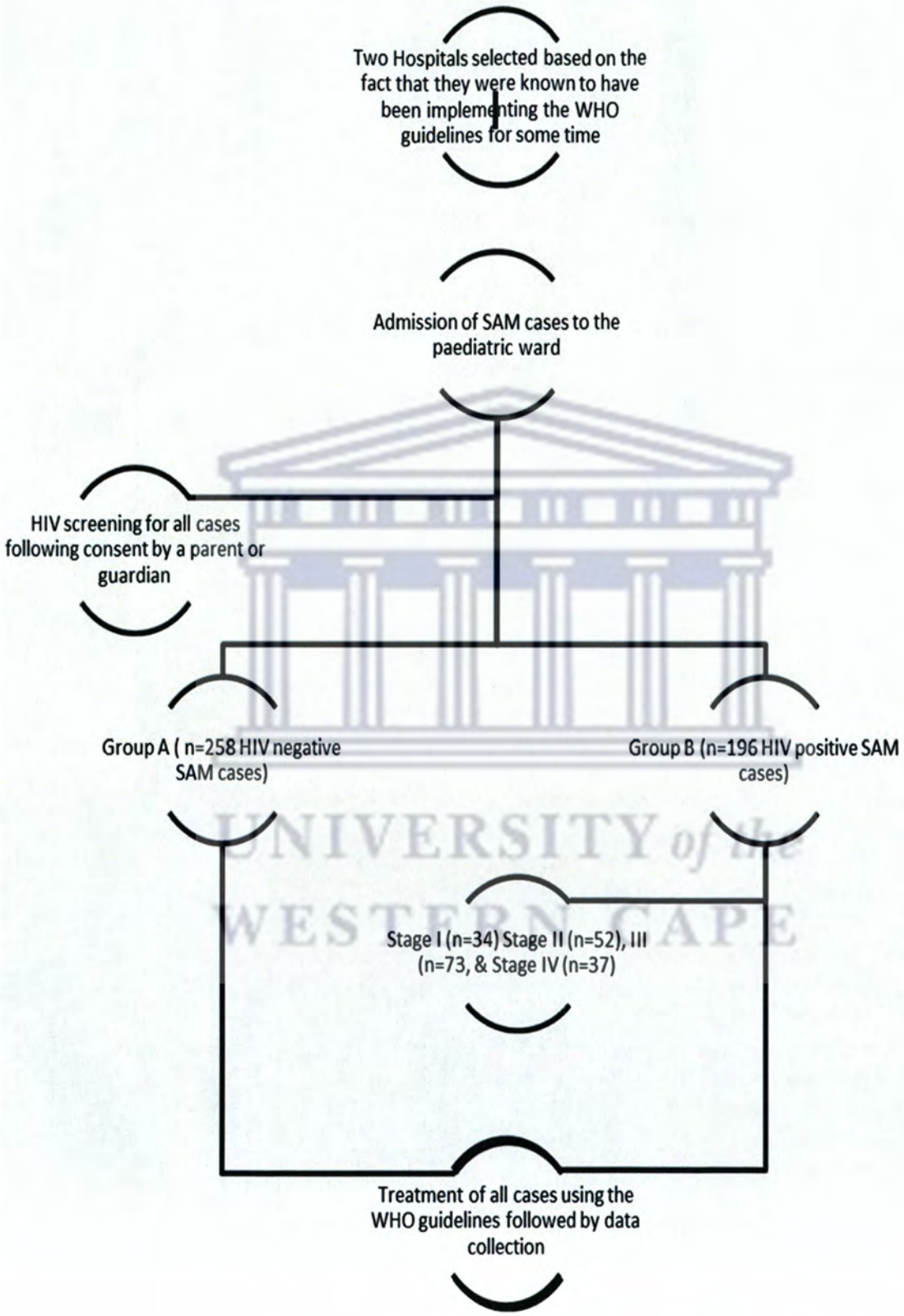

Figure 10: *Flow chart for participant recruitment during Phase 2 of the study*

4. 8.3. Variable definition and measurement

4. 8.3.1. Exposure variable

All the cases that were included in the study were admitted with SAM which was considered as the main exposure variable. Severe acute malnutrition was defined as per the WHO criteria which recognises SAM as: (1) a weight-for-height measurement of 70% or more below the median or 3 standard deviations (SD) or more below the mean National Centre for Health Statistics reference values (also called "*wasting*"), or (2) the presence of bilateral pitting oedema of nutritional origin, which is called "*oedematous malnutrition*" (Collins et al, 2006). Based on this definition, the researcher used the corresponding nomenclature in the Wellcome classification (Hendrickse, 1991) to standardise data for the sake of data analysis. For example, children classified as wasted by the doctor using the WHO criteria were reclassified as marasmic to suit the Wellcome nomenclature. Those who had oedematous malnutrition without a degree of wasting were considered to have kwashiorkor, where those who were oedematous and had signs of wasting were classified as having marasmic kwashiorkor. However, this classification has been superseded by the new WHO classification, although it is still used widely in clinical practice.

The mid-upper arm circumference (MUAC) of less than 110 mm, which is an alternative definition of SAM, is not considered here as it was not measured in this study.

Severe acute malnutrition was further subdivided in three different syndromes namely: kwashiorkor (oedematous malnutrition), marasmus (severe wasting), and marasmic kwashiorkor (severe wasting with oedema) (Puoane at al. 2006). In addition to constituting the exposure variable (SAM), these three syndromic variants of SAM were also treated independently as predictor variables during statistical analyses.

4. 8.3.2. Outcome variables

Three outcome variables were measured in Phase 2. The first variable was ***Survival***, which was defined as a binary variable consisting of two categories (*Death* while on treatment and *Discharged* following treatment). There were only 12 SAM cases that *defaulted* or *absconded* treatment. These were excluded from the analysis as they would have biased some statistical estimates involving some variables such as the duration of hospitalisation. The second outcome variable was ***Duration of hospitalisation*** while on treatment which was a function of survival. This was a continuous variable defined as the number of days spent in the hospital from admission to death or from admission to discharge. The third and last outcome variable was *the **Rate of weight gain*** while on F100. This variable was defined as the number of grams gained per kilogram of body weight per day during the rehabilitation phase. Using a hypothetical SAM case, Box 3 below illustrates how a standardised formula was used to calculate the rate of weight gain.

Example of Mary

Day 6 (weight 1) = 3.7kg
Day 16 (weight 2) = 4.3kg

1. **Calculate the weight gain in grams**
   Subtract the first weight from the second weight = **0.6kg (×1000= 600g)**

2. **Calculate the number of days between the two weights**
   In this example it is from day 6 to day 16=**10 days**

3. **Divide the weight gain by the number of days to get g/day**
   In this example it is **600g divided by 10 days which is 60g/day**

4. **Take the average of the two weights**
   Add the two weights and divide by 2. In this example it is 3.7+**4.3/2=4.0kg**

5. **Divide the weight gain/day divided by the average weight**
   In this example it is **60g/day divided by 4.0kg=15g/kg/day**

Box 3: *Hypothetical example of how the estimates of rate of weight gain were obtained*

Cases with the rate of weight gain **≤ *0g/kg/day*** were considered as having had a declining weight or no weight gain, whereas those with **≤ *5g/kg/day*** had poor weight gain, **5-10g/kg/day** had moderate weight gain and **>10g/kg/day** had good weight gain. There were four cases with negative estimates of the rate of weight gain but these were not included in the analysis mainly because they were too few (0.8% of the total sample size) and and their inclusion would have skewed the locally

weighted means using in the polynomial two-way scatter plots in Figures 33 and 34, as well as the box and whisker plots for involving the 'rate of weight gain' variable.

4. 8.3.3. Predictor variables, confounders and effect modifiers

Only the factors that were presumed clinically relevant to the study were considered as predictor variables, confounders or effect modifiers. The variable was defined as a potential confounder if, when included in the analysis, distorted the association between the primary predictors and the outcome of interest. On the other hand, an effect modifier was defined as a variable which when, included in the interaction term with another variable, affected positively or negatively the magnitude of the effect of the primary predictor on an outcome of interest (Kamangar, 2012). These factors are defined in Table 2 below. Here, the primary predictors are illustrated by the symbol Ⓟ, possible confounders by the symbol □ and effect modifiers by the symbol Δ.

Table 2: *List of predictor variables, confounders, and effect modifiers and their definitions in the study*

Variable	levels or categories	Definition and methods of assessment
□ ***Hospital Name***	St Patrick's Hospital	These were defined as the facilities in which children were admitted and treated
	Holy Cross Hospital	
□ ***Age***	Continuous variable	Age ranged from 6 - 60 months
Ⓟ ***Oedema Grade*** *(WHO/UNICEF, 2009)*	Nil	No presence of oedema
	Mild Oedema (+)	Oedema of nutritional origin on both feet
	Moderate Oedema (++)	Oedema of nutritional origin on both feet, plus lower legs, hands or lower arms

	Severe Oedema(+++)	Generalised Oedema of nutritional origin including both feet, legs, hands, arms and face
Ⓟ *Dermatosis Grade (Latham, 1991)*	Nil	No Dermatosis present
	Mild Dermatosis (+)	Discolouration or a few rough patches on the skin
	Moderate Dermatosis (++)	Multiple patches on arms and/or legs
	Severe Dermatosis (+++)	Flaking, raw skin, fissures
Δ *Presence of respiratory tract infection (LRTI or TB)*	Yes	Lower Respiratory Tract Infections (LRTI) was an umbrella term for cases with comorbidities such as pneumonia, bronchitis and other infections below the larynx which are commonly noted by doctors in both hospitals. Tuberculosis was also categorised as a respiratory tract condition even though it was not common
	No	
Δ *Child critically ill on admission*	Yes	Definition of a case as "critically ill" was based on whether or not they were admitted with one or a combination of five clinical features namely: (1) Depressed conscious state (prostration or coma), (2) Bradycardia, (3) Evidence of shock with or without dehydration (4) Hypoglycaemia and (5) hypothermia. These clinical manifestations have been documented as the strongest predictors of early death (death within 24 hours) of admission (Maitland et al. 2006).
	No	
Δ *Presence of other comorbidities on admission*	Yes	"Other comorbidities" were conditions directly or indirectly related to SAM and documented in the literature as moderate risk factors of death among severely malnourished children (Maitland et al. 2006) excluding LRTIs, TB, HIV/AIDS and other conditions associated with critical illness as described above. This category of predictors included for example: lethargy, hyponatraemia and hypokalaemia, dehydration, deep acidotic breathing, anaemia and pyrexia, herbal intoxication, presence diarrhoea, burns and other hereditary dysfunctions commonly reported by the doctors in each hospital.
	No	
Ⓟ *HIV Test Results*	Positive	HIV status was determined as per the WHO guidelines (WHO, 2005)
	Negative	
Ⓟ *WHO HIV/AIDS disease stage*	Stage IV	HIV disease stages were determined as per the WHO guidelines (WHO, 2005)
	Stage III	
	Stage II	
	Stage I	
	N/A	
Ⓟ *Quality of clinical care*	Continuous variable	Quality of clinical care was defined as the extent to which a number of treatment steps promulgated in the WHO guidelines were implemented as applicable for a particular case. This was expressed as a score ranging from 0 (Step not appropriately followed) to 1 (Step appropriately followed).

		Overall, there were 60 steps which fell under 8 broad themes (See Table 3). However, the extent of application of these steps varied according to the condition of an individual case. For example not all cases required treatment of shock and therefore, for that particular case, the protocol for treatment of shock was not taken into account when scoring the quality of care

Table 3: *Thematic indicators used to assess the quality of clinical care for SAM and the number of observations made under each indicator*

Thematic indicators of quality of care	n (pooled)
1. Score for treatment and prevention of hypoglycaemia	454
2. Score for treatment of infection	454
3. Score for electrolyte imbalance & micronutrient deficiency	454
4. Score for management of rehydration	404
5. Score for treatment of shock	140
6. Score for blood transfusion	75
7. Score for patient monitoring	450
8. Score for appropriate patient discharge procedure	334

The quality of clinical care consisted of 60 individual quality-of-care indicators (See Appendix 9) which reflected the minimum steps drawn from the WHO treatment modality that should have been followed by the health care worker to treat all patients. Each of the 60 indicators of health care was first evaluated independently during data collection. At this stage, each quality care indicator was scored 0 or 1 depending on whether it was satisfactorily implemented and as required to treat the patient (0= unsatisfactory or 1= satisfactory). The height for weight and weigh for age Z-scores were not included in the variable list. There were some inconsistencies in how information on individual anthropometric measurements such as height and

weight was recorded by different nurses at both facilities. However, classification of nutritional status (severe vs. moderate, marasmus vs. kwashiorkor and a combination of both) was done in the outpatient department by the consulting doctor based on the WHO definition stated in Table 2. Cases whose definitions of SAM status were not clear or were not noted by the doctor in the patient record were further checked with the nurse before inclusion in the study. The lack of this information was largely due to misplaced sheets on which patient diagnosis was recorded or illegible notes from the doctor. In the case of the missing sheet, the researcher asked the nurse whether the sheet could be located for that particular case. Where this was not possible, the case was excluded from the study. For illegible notes, the researcher also asked the nurse to sick clarification from the doctor who consulted on the child or the nurse to assist if she was aware of what was written.

Furthermore, the Mid Upper Arm Circumference (MUAC) was not routinely measured in the hospital and thus it was not used to define SAM in this study.

4. 8.3.4. Criteria against which the management of HIV infection for SAM cases was assessed

- Children with SAM and HIV co-infection were diagnosed at the Hospital and referred to an HIV clinic situated within the hospital premises for initial treatment and follow up based on the following WHO treatment guidelines (WHO 1999).
- All HIV-infected infants and children who were less than 24 months of age were initiated with lifelong antiretroviral drug treatment, irrespective of

clinical staging (including severe acute malnutrition) and CD4 count. Co-trimoxazole prophylaxis was also initiated;

- All HIV-infected SAM cases that were over 24 months and less than 5 years of age were started on lifelong antiretroviral drug treatment based on their CD4 count (≤750 cells/mm3) or CD4 percentage (antiretroviral drhad WHO clinical staging 3 or 4 (including severe acute malnutrition).
- Children with severe acute malnutrition who were HIV infected and who qualified for lifelong antiretroviral therapy were started on antiretroviral drug treatment as soon as possible after stabilization of metabolic complications and sepsis
- Additional guidelines that related to toxicity and other additional complex presentation are outlined in the WHO treatment guidelines (WHO 1999).

4. 8.4. Data collection tools and procedure

All the data in Phase 2 of the study were collected through data extraction from patient records which are routinely kept in the ward for reference when required. Record reviews were conducted three monthly during scheduled hospital visits and over a period of 53 months (from January 2009 to May 2013).

Data extraction from patient records was done using a 76-item pre-tested and standardised patient evaluation form originally developed by the International Malnutrition Taskforce and Muhimbili Hospital in Tanzania (WHO, 2010). The tool was slightly modified to conform to the standards and context of the study setting (See Appendix 9). The modification involved separation of the patient record section

from the ward observation sections. The latter was used ad hoc during the ethnographic enquiry. The definitions and methods of assessment for each of the extracted variables have been described earlier in Table 2.

As discussed above, ideally a SAM case brought to any of the two hospitals was seen by a doctor in the outpatient department. At this point, the admitting doctor provided the diagnosis and the course of treatment to be followed based on the WHO guidelines. This information was recorded in the patient treatment folder as the basis for follow-up treatment and for the purpose of record keeping. Upon admission to the ward, mothers or guardians of all the children were requested to provide consent so that their children would be screened for HIV infection. HIV Testing and Counselling (or Human Testing and Counselling) were performed by a professionally trained nurse. All blood samples were sent to an in-house pathology laboratory for all relevant haematological evaluations. Children who tested HIV positive were identified and their folders set aside by a senior nurse for HIV disease staging during follow-up visits. HIV disease staging was performed by the ward doctors in each hospital

During hospital visits, the researcher worked with the resident senior nurse to identify all patient folders for cases that met the inclusion criteria for the study. Each patient folder was thoroughly reviewed by the researcher and where some information was not clear, the researcher contacted the clinical team in the ward for clarity. For each visit, cases admitted and treated during the three months since the last visit were reviewed.

4. 8.5. Data validity and reliability

The whole data collection process during Phase 2 was standardised in both hospitals. In order to ensure that all the data collected were accurate, accessible when required, reliable, precise and comprehensive, standard operating procedures (SOPs) were adopted and sustained through regular feedback and update with the clinical staff. For example, the patient treatment folders contained standardised treatment charts for the clinical staff to remember what to do as part of treatment and the researcher to be able to gather all the required information for the research. These tools were described earlier and are presented in Appendices 10 to 15.

Throughout the entire study period, data collection and abstraction were done by one researcher (the PhD candidate) who was external to the two hospitals. The researcher had a clinical nutrition background and was familiar with the WHO treatment modality for SAM, including the context of treatment. However, it is important to highlight that even though all possible measures were put in place to ensure that the information recorded in the patient folder was of high quality, this may not have been the case throughout the study period. One potential threat assumed to have affected data validity (completeness, correctness, accuracy, consistency, and appropriateness) during Phase 2 was measurement bias. This kind of threat to data validity has been documented before in similar study designs (Thiru, Hassey and Sullivan, 2003). It is possible that the information collected over time from different cases may have been measured and recorded by multiple individuals with varying professional attributes, thereby introducing some inconsistencies in the validity of the measurements. Efforts to ensure fidelity of the

measurements involved standardisation of measurement techniques whereby for example the formular for preparation of feeds were put up in the kitchen for nurses to refer to when preparing feeds or rehydration solutions, demonstrations on how to calibrate the baby weight electronic measurement scales (A&D, 2011), and how to use other drug administration charts. These included standardised dosage charts to use during the administration of antibiotics, multivitamins, electrolytes and ARV's as applicable (Appendix 10); fluid administration charts to record the amount of F75 and F100 given and left over (Appendix 11), An output chart to keep track of the patterns of diarrhoea, vomiting and urine discharge (Appendix 12); weight monitoring chart to monitor the rate of weight gain (Appendix 13); Four hourly temperature and pulse monitoring chart (Appendix 14); as well as the Oral Rehydration Solution (ORSOL) chart to document the rehydration procedure followed during patient management (Appendix 15). Demonstrations were generally done on an ongoing basis with nurses who had not received an induction on the use of the WHO treatment guidelines. This exercise was further reinforced through other mechanisms described earlier as key components of the revised intervention.

4. 8.6. Data management

After data collection, all the patient evaluation questionnaires were coded for data capturing. Data from both hospitals were captured in one Excel spreadsheet. A variable called *hospital name* was created to ensure that data from each hospital could be distinguished during data analysis. Initial data cleaning was done in Microsoft Excel following data capturing. The resultant Excel dataset was imported into

Stata/IC 13.0 (Statacorp, 2013) for more advanced data cleaning, as well as variable coding, labelling and transformation. All the errors and missing information identified during data cleaning were rectified by rechecking the parent questionnaires. The final Stata dataset was then used for data analysis in Stata/IC 13.0.

4.8.7. Data analyses

4.8.7.1. Descriptive analyses

Descriptive analyses involved characterisation of the responses in the patient evaluation questionnaire by computing summary statistics such as mean, median, frequencies, interquartile ranges, standard errors and standard deviations. Graphical presentations including bar graphs Histograms and Box and Whisker plots were also used where applicable to summarise data.

4. 8.7.2. Inferential analyses

Generally, the data were not normally distributed so non-parametric tests were used for the most part. Where groups were compared on the basis of categorical explanatory variables, Pearson's Chi Square or Fisher's exact tests were computed. To compare groups on the basis of continuous dependant variables, the Mann-Whitney U and Kruskal-Wallis non-parametric tests as well as the t-test were used as applicable.

Kaplan-Meier Failure (death) curves and hazard functions were plotted to depict survival prospects of severely malnourished children based on their HIV status and

disease stage (for those who were HIV positive). Log-rank tests for equality of failure functions were also computed to determine whether the hazard curves and functions were statistically significant.

In order to determine the predictors of survival among children admitted with SAM to both hospitals, a univariate (Crude) Cox Non-parametric Proportional Hazard Model was first constructed. All the variables, be it categorical or continuous, which were presumed to be of clinical relevance to survival were entered in the model singly until all of them had been evaluated. For categorical variables, Hazard Ratio (HR) estimates with the 95% confidence intervals as well as p values were computed. For continuous variables, parameter estimates (β coefficients) were obtained with the 95% confidence intervals and p values. Categorical variables evaluated in the univariate model were hospital, age category, SAM syndromic variants, oedema grade, dermatosis grade, presence of LRTIs, presence of other comorbidities, critically ill on admission, HIV status and disease stage. Continuous variables were the quality of clinical care and the rate of weight gain.

Since the quality of clinical care was a multifaceted variable, it was important to first transform it before entering it in the Cox model. The quality of clinical care consisted of 60 individual quality-of-care indicators which were first evaluated independently during data collection. At this stage, each quality care indicator was scored 0 or 1 depending on whether it was satisfactorily implemented and as required to treat the patient (0= unsatisfactory or 1= satisfactory). During data analysis, all the individual scores for each indicator were aggregated as applicable to constitute 8 thematic indicators of quality of clinical care (Table 3). This was a preliminary step performed

as part of the data reduction procedure. The 8 thematic indicators of quality of care were further reduced to an overall composite score using a multivariate data reduction technique called Principal Component Analysis (PCA) (Ringner, 2008).

The PCA was used to construct a weighted quality of clinical care score which was later used in the risk factor analysis. The composite score was very useful as individual scores were highly co-linear with a large variance inflation factors (VIF), and thus could not be included in the adjusted multivariate model. The component score for each of the 8 thematic quality-of-care indicators was summed to give an overall continuous quality of care composite score with lower (negative) values representing poorer quality of care and conversely for higher (positive) scores (See appendix 16). However, only component scores for management of hypoglycaemia, treatment of infections, correction of electrolyte imbalance, and management of micronutrient deficiency as well as monitoring of patient treatment progress were used to create a weighted composite score for quality-of-care. Other quality-of-care indicators had substantial missing values (see totals in Table 3) as some of them were not applicable to every case treated. Therefore, they were not included in the overall composite score. Since the quality of care score was a continuous variable, a covariate adjustment method was required to estimate the hazard ratios. The hazard ratios were estimated by comparing units of the quality care composite score. The hazard ratio was interpreted as a ratio of hazard comparing cases differing by one unit, at risk of death, holding other variables constant.

Model building for the multivariate (Adjusted) Cox Non-parametric Proportional Hazard Model involved selecting all the variables which were statistically significant

($p<0.05$) at univariate level and entering them into the model to determine which factors best fitted the overall model. Potential confounders were also identified at multivariate level. The overall model was subjected to further test to check whether it did not significantly violate the proportional hazards assumptions based on a $p>0.05$ cut-off. The Cox formulation was also used to quantify the impact of the interaction of factors on survival prospects of study subjects and also to identify potential effect modifiers.

To assess the relationship between mean rate of weight gain and duration of hospitalisation at different time intervals, the non-parametric locally-weighted regression using a scatterplot smoothing technique was used. The mean rates of weight gain were weighted based on the number of all SAM cases present in the hospital within a two-day interval, and then *successively* until the last day of hospitalisation recorded.

Comparison of the rate of weight gain across SAM categories, and HIV disease stages was done using the Kruskal-Wallis test. To compare differences in the rate of weight gain between various pairs of HIV disease stage, the two-sample Wilcoxon rank-sum test was used. The same test was also used to compare differences in duration of hospitalisation between the two hospitals. Multiple comparisons of between-hospital differences in terms of different clinical characteristics were computed using post-hoc non-parametric tests. All the comparisons were graphically presented using box and whisker plots. Throughout the analysis a p value of less than 0.05 was considered statistical significant.

PHASE THREE

4.9. Evaluation of the sustainability of the revised intervention

Phase 3 of the study started in 2013 with a retrospective assessment of the hospitals' performance in reducing monthly death rates related to SAM during and after the *revised* intervention described in Figure 9. As explained below, this phase consisted of two complementary quasi-experimental designs for quantitative impact evaluation.

4. 9.1. Study designs

Phase 3 involved the use of an interrupted time series design. Time series is a term which refers to a large series of observations made on the same variable consecutively over time (Shadish, Cook and Campbell, 2004). An interrupted time series is a type of time series design which has been shown to be a strong quasi-experimental alternative of randomised control trials when the latter is not feasible to conduct and data on time series is available (Biglan, Metzler, & Ary, 1994). Some scientists have also argued that the interrupted time series design is the strongest quasi-experimental design that can be used to evaluate longitudinal effects of time-defined interventions (Cook, Campbell, 1979; Gillings, Makuc, Siegel, 1981).

Interrupted time series designs usually involve the measurement of a variable (or variables) of interest before and after the introduction of specific interventions to assess whether the interventions has had an impact on that variable over time (Gillings, Makuc and Siegel, 1981). The impact of the intervention can then be

measured by assessing the level and trend (slope) changes of that variable over time, which are presumed to be affected by the presence of the intervention alone.

During the third phase of this study, the researcher used the same concept to assess whether discontinuing a longstanding intervention, as opposed to introducing it, would have an effect on the level and trends of three performance indicators of mortality which are explained later in this chapter. The resultant study design was therefore an interrupted time series design with an embedded *"removed intervention design"*. This approach was applied to time series data from each hospital so that results could be compared thereby enhancing study validity.

The aim of the *removed intervention design* is to demonstrate that the outcomes improve and worsen with the presence or absence of Intervention – a result that could be otherwise explained only by a threat to validity that similarly rose and fell over the same time (Shadish, Cook, Campbell, 2004). The researcher's aim was to determine the sustainability of the *revised* intervention after system-strengthening and supportive supervision components of the intervention (darker-shaded components in Figure 9) had been discontinued in August 2011. After August 2011, the hospitals were managing SAM cases independently without support from the research team. Therefore any performance realised during this period would be a fair reflection of the sustainability of the intervention.

The discontinuation of the revised intervention in 2011 was solely a result of the end of the funding period. Box 4 below illustrates the components of a removed

intervention design used in this study. The hypothesis underlying this design has been stated in Chapter 1.

O_1	X	O_2 ..... O_{n1}	$\cancel{X}$	O_3 ..... O_{n2}			
Where:							
O_1	:	*Baseline observation before introduction of the full intervention (Jan 2009)*					
X	:	*Introduction of the full intervention (Jan 2009)*					
O_2.....O_{n1}	:	*32 post-intervention observations measured monthly (Feb 2009 – Aug 2011)*					
$\cancel{X}$	:	*Discontinuation of the intervention in August 2011*					
O_3.....O_{n2}	:	*37 post-discontinuation observations measured monthly from (Aug 2012 – Sep 2014)*					

Box 4: *Interrupted Time Series design with an embedded Removed Intervention Design*

4.9.2. Parameter definition

In both study facilities, 69 monthly data points (time series) were measured on three of the nine routinely documented hospital-level performance indicators related to the management of SAM. The three indicators were: 1) *Total monthly deaths due to SAM*, 2) *Monthly SAM deaths during the first 24 hours of admission*, and 3) *Monthly number of deaths attributable to SAM and HIV infection*. The data points were for the period January 2009 to September 2014.

The parameters used to evaluate the three performance metrics were defined using Wegner's guidelines for segmented regression analysis of interrupted time series research (Wegner et al, 2001). A *time series* was defined as a sequence of values for

each performance indicator taken at evenly spaced intervals between January 2009 and September 2014. The sequence of these values was divided into two portions, namely *segments* and the *change points*. The *change points* were defined as specific points in the time series where the values for each performance metric exhibited a change as a result of the discontinuation of the revised intervention.

Two parameters namely *level* and *trend* were used to define each segment of a time series. Wegner et al. (2002) defined the *level* as the actual value of the series (in this study referred to as the value of the performance metric (e.g. Number of deaths attributable to SAM) at the beginning of a given time interval. In this study, the *trend* was defined as the rate of change of a given performance metric during a segment (Wegner et al., 2002).

4.9.3. Data collection

At the beginning of the study, a performance monitoring tool (Appendix 17) was developed for use by the two hospitals. As described earlier, the tool contained nine performance metrics including the three which were measured in this study. A senior nurse based in the paediatric ward in each hospital was assigned to measure and record each of these metrics at the end of each month. The nurses were trained by the research team on how to calculate and record these metrics on a monthly basis so that they conform to the research design and standards. The research team consisted of the PhD candidate himself and his supervisor, a Professor of public health who was the co - principal investigator of the study when it was launched in 1999. It was important to inform the two nurses from the two hospitals that the

information had to be recorded as accurately as possible and that it would not be used for any purpose other than research.

All the data were collected retrospectively by the researcher. The first wave of data collection was completed in July 2013 and the second one in September 2014. The collected data were entered directly into a structured data collection template and thereafter verified by the researcher with the help of the nurse to rectify the statistics which looked odd (Appendix 18).

4.9.4. Data management

Data from both hospitals were captured in two separate Excel databases. The data were then structured for analysis using the guidelines by Wegner et al. (2002) on the segmented regression analysis for time series data. This data structure (Appendix 19) consisted of four other variables against which each performance metric was regressed. The four values were:

1) *Intervention discontinuation variable* - which was a dummy variable taking the values 0 in the pre- intervention discontinuation segment and 1 in the post- intervention discontinuation segment;
2) *Time after intervention discontinuation variable* - which took the value 0 in the pre-intervention discontinuation segment and counts the months in the post-intervention discontinuation segment at time *t* (32…69),
3) The *time* variable which denoted all the months for the entire time series, starting with the time when the time series started (January 2009) to when it was interrupted (August 2011) and stopped (September 2014), and

4) The *observation* variable which was a series of numbers (1 to 69) representing successive numbers of data points in the time series. The resultant datasets were then imported in Stata/IC 13.0 (Statacorp 2013) for analysis.

4.9.5. Data analysis

Segmented regression analysis, an interrupted time series technique proposed by Wegner et al. (2002), was used. Analysis was aimed at estimating the level and trend changes in the pre- intervention discontinuation segment and the changes in level and trend following the discontinuation of the revised intervention.

The segmented Poisson regression model fitted to the data was given by the formula:

$$Y_t = A_0 + A_1 \times \text{time}_t + A_2 \times \text{intervention discontinuation}_t + A_3 \times \text{time after intervention discontinuation}_t + e_t$$

Where:

- Y_t represented the performance metric of interest (e.g. total number of monthly deaths due to SAM),
- A_0 estimated the baseline level of the performance metric at time = zero (January 2009),
- A_1 estimated the change in the performance metric that occurred with each month before the revised intervention was interrupted (i.e. baseline trend),
- $Time_t$ was a continuous variable indicating time in months from the start of the observation period,

- A_2 estimated the level change in the performance metric immediately after the discontinuation of the revised intervention,
- ***Intervention discontinuation*** $_t$ was an indicator for time t occurring before or after the discontinuation of the revised intervention,
- A_3 estimated the trend in the performance metric after the discontinuation of the revised intervention,
- ***Time after intervention discontinuation*** $_t$ is a continuous variable counting the number of months after the discontinuation of the revised intervention at time t, and
- e_t represented the random variation not explained by the model.

As all the performance metrics consisted of count data, Poisson Regression was used instead of the standard linear regression proposed by Wegner et al. (2002). The exponentiated model coefficients from Poisson regression were more perceptible and a lot more sensible to interpret.

Poisson regression was also more suitable as it allowed for all the performance metrics to be assessed relative to the common denominator (total number of admissions due to SAM) in the segmented regression model. Therefore, in the segmented regression model, each of the three performance metrics reflected the number of deaths recorded in each month (e.g. Number of SAM deaths within 24 hours of admission) divided by the number of SAM cases admitted in that month who were at risk of dying. The resultant estimate was reported as a monthly mortality rate per 1,000 children admitted. The month to month change in each performance metric was reported as the Incidence Rate Ratio (IRR). Line graphs

were also used to visually inspect the series over time. The graphs were constructed so that for each performance metric they depicted the trend and level changes from the *observed monthly mortality rates,* and the trend and level change from the *model-predicted mortality rate* derived from the exponentiated regression coefficients. The parameter estimates from the regression model and the line plots for each performance metric were compared between the two hospitals to assess whether there were similarities in findings.

Box 5 summarises the different statistical tests and graphs used for descriptive and inferential analyses of Phases 2 and 3 data.

Test statistic Graphical representation	Data analysed
Descriptive analyses	
• ***Means, medians, frequencies, interquartile ranges, standard errors and standard deviations***	Characterisation of continuous response variables in the patient evaluation questionnaire
• ***Histograms with normal density plots***	To examine the skewness and normality of numerical data
• ***Box and Whisker Plots***	To examine the distribution of numerical data across various categories
• ***Divergent Bar Graph***	To examine the distribution of a numerical variable across a categorical variable
Inferential analyses	
• ***Pearson's Chi Square or Fisher's exact tests***	To compare the frequency of cases in the various categories of one variable across the different categories of another variable
• ***Mann-Whitney U test***	To test for differences between two independent groups (e.g. HIV status) on a continuous measure (e.g. rate of weight gain)
• ***T-test***	To compare the mean score some continuous variables (e.g. mean duration of hospitalisation between the two hospitals)
• ***Two-sample Wilcoxon rank-sum test***	To compare differences in the rate of weight gain between various pairs of HIV disease stage and the differences in duration of hospitalisation between the two hospitals
• ***Kruskal-Wallis test***	To compare the scores on some continuous variable (e.g. rate of weight gain, duration of hospitalisation) for three or more Groups (e.g. SAM syndromic class, HIV disease stage)
• ***Kaplan-Meier Failure (death) curves with hazard functions***	To depict survival prospects of severely malnourished children based on their HIV status and disease stage (for those who were HIV positive)
• ***Log-rank tests for equality of failure functions***	To determine whether the hazard curves and functions were statistically significant
• ***Univariate and multivariate Cox Non-parametric Proportional Hazard Model with Hazard Ratio (HR) estimates and 95% confidence intervals***	To determine the predictors of survival among children admitted with SAM to both hospitals
• ***Principal Component Analysis (PCA)***	To reduce data in respect of the quality of care score and to generate the weighted quality of clinical care score
• ***Non-parametric locally-weighted regression using a scatterplot smoothing technique***	To assess the relationship between mean rate of weight gain and duration of hospitalisation at different time intervals
• ***Segmented Poisson Regression Analysis***	To estimate the level and trend changes in the pre- intervention discontinuation segment and the changes in level and trend following the discontinuation of the revised intervention
• ***Line graphs with observed and model-predicted line plots***	To visually inspect mortality trends over time

Box 5: *Summary of test statistics used to analyse Phases 2 and 3 Data*

PHASE FOUR

4. 10. Contextualisation and explanation of the quantitative findings

This section outlines two methodological approaches used during Phase 4 of the study. The section is divided into two parts. The first part outlines the research process followed during an ethnographic enquiry which started at the beginning of the study and was concluded in May 2013 when the study intervention was discontinued. The second part describes how FGDs were conducted at the end of the study in May 2014 to put quantitative findings into context. Generally, both parts complemented each other despite the fact that they consisted of different research designs and were conducted during unequal time intervals.

PART ONE

4. 10.1. Focus Group Discussions

Focus group discussions have, increasingly, been advocated in medical and public health research (Liefooghe et al, 1995). A focus group usually takes the form of a 'group interview' which focuses on a particular research topic of interest and is facilitated by a researcher (Baum, 1999). This method of qualitative data collection can be used to generate thick information on beliefs, values and understanding of issues related to a particular phenomenon of interest (Liefooghe et al, 1995).

Some proponents of FGDs have argued that this method can encourage participation from individuals who may be reluctant to be interviewed individually (Marshall & Rossman, 1999). However, other researchers have expressed concerns that if poorly

organised and participants are not appropriately selected, FGDs can lead to some individuals in the group being discouraged from participation if they feel their opinion is trivial or different from the majority in the group (Kitinger, 1995). Therefore, it is critical to be mindful of this potential threat to data quality when planning and conducting FGDs.

The purpose of the FGDs was to elicit information from participants about their views on and interpretation of the quantitative findings as well as the context thereof based on their day-to-day experiences managing SAM cases in their respective hospitals. Key assumptions posited in the intervention theory of change (See Table 1) at the beginning of the study were also explored during FGDs. Some issues that were noted but not clarified during the observation period were also explored during FGDs.

4. 10.1.1 Selection of Focus Group Participants

Two specifications were considered in determining focus group compositions. These were: (a) the basic composition of the groups (homogeneous versus heterogeneous) and (b) the professional profile of the participants.

Selection of participants based on these two specifications was central to the achievement of the study objectives. The researcher was mindful of the fact that in order for the participants to share their ideas to the maximum extent possible, it was important to establish a climate of mutual respect within the group. Therefore, in each hospital, two FGDs were held, each with a different target population, in order to achieve group homogeneity. One group consisted of a mixture of the senior

clinical personnel and senior staff from the hospital management cluster. The other group consisted mostly of relatively junior clinical staff in the nursing category. Table 4 below outlines the number and designations of the participants who were part of the FGDs in each hospital.

The homogeneous nature of the FGDs had the potential to alleviate the likelihood of intragroup disagreements based on a number of participants' attributes and profile (e.g. professional status and seniority in the facility). The uniform composition of the groups therefore delivered insights that are representative of the target population (Hines, 2013).

4. 10.1.2. Data collection for focus groups

A personalised invitation (Appendix 22 and 23) to participate in FGDs was sent to each hospital in May 2014, one month before the visit. The letter was addressed to the hospital manager/CEO and specified the purpose of the FGDs, the profile of the participants required and the dates and times for each focus group session. On the day of data collection, and few minutes before focus groups were held, all the participants received information sheets (Appendix 5 and 6) explaining the research purpose and what the focus groups entailed. They were also requested to voluntarily hand-sign a consent form (Appendix 7 and 8) which confirmed their voluntary and informed participation in the study.

Table 4: *List of participants from each hospital who took part in the FGDs*

HOLY CROSS HOSPITAL			
Senior clinical and management team	***n***	**Junior clinical staff**	***n***
Medical Officer (MO)	1	Staff nurse	4
Dietician	1	Junior nurse	1
Pharmacist	1	Professional nurse	2
Social worker	1		
Nursing service manager	1		
Paediatric nurse	1		
Assistant manager – nursing	1		
Area manager – maternity	1		
Infection control coordinator	1		
Operational manager on behalf of the CEO	1		
TOTAL	**10**		**7**

ST PATRICK'S HOSPITAL			
Senior clinical and management team	***n***	**Junior clinical staff**	***n***
Nursing service manager	1	Ward nurse	3
Medical Officer (MO)	2	Student nurse	1
Social worker	1	Professional nurse	1
Dietician	1		
Pharmacist	2		
Deputy director – clinical services	1		
Quality assurance officer	1		
Operations manager	1		
Hospital administrator	1		
TOTAL	**11**		**5**

The FGDs were structured and conducted as per the guidelines by Krueger (1994). The researcher first emphasized the importance of making each other feel comfortable and relaxed, and then outlined the focus group proceedings and rules, particularly the issue of confidentiality and honesty. All the discussions were conducted in English language which most participants spoke and understood well. However, there were no restrictions regarding the use of the local language.

The discussions started with an outline of the quantitative findings which provided a platform for participants to reflect on the performance of the hospital regarding the management of SAM over the entire study period. The researcher, who was also the FGD facilitator, ensured that the presentation of quantitative findings was pitched to the level of the audience so as to maximise participants' feedback. The presentation was then followed by a series of unstructured questions (Appendix 24) developed in such a way that each question related to a specific aspect of the quantitative findings. Probes were interjected in-between participants' responses to elicit richer qualitative insights into the subject matter and to provide the context thereof.

4. 10.1.3. Data analysis for FGDs

The first step of analysing focus group data involved verbatim transcription of all the interviews using Microsoft word processor. The interviews were transcribed separately so that the findings could be compared between the hospitals. The second step entailed the use of the 'Framework Analysis Technique" to analyse all the transcribed data. According to Pope, Ziebland, and Mays (2000), framework analysis is a qualitative analysis technique which is geared towards generating policy and

practice oriented findings. The technique has many advantages including the fact that it preserves the integrity of individual responses throughout the analytical process, thereby providing a platform for reconsidering and reworking of ideas where more clarity is needed (Bryman and Burgess, 1994). The analysis usually involves a systematic process of sifting, charting and sorting materials according to key issues and themes (Pope, Ziebland, and Mays, 2000).

During the second step of data analysis, the researcher immersed himself in the raw data (familiarisation phase) by reading transcripts and studying notes in order to identify key ideas and recurrent themes. The researcher then identified all the key issues, concepts and themes by which the data could be referenced. This was done by building on the questions derived from the aims and objective of the study and the issues that emerged during focus group discussions. The end product of this process was a detailed index of the data which labelled the data into manageable chunks. A thematic framework was then applied to the data in the individual transcripts by using numerical codes from the index with short texts describing the index heading. Finally, the data were mapped and interpreted by defining concepts, creating typologies and finding the relationship between themes in order to obtain an explanation for the findings.

PART TWO

4.10.2. Ethnographic inquiry

According to Emerson (1995), Ethnographic field research involves the study of cultures, organisations and societies by observing groups of people as they go about

their everyday lives. The ethnographer does this by entering the social setting and "getting close" to the people in it and making specific observations relating to a particular phenomenon as it unfolds (Emerson, 1995). The ethnographic enquiry was aimed at observing and recording information about the behaviours, activities, events and other aspects relating to the implementation of the study intervention throughout the study period. This was done using field notes which have been defined by Burgess (1991) as transcribed notes or the written account obtained from observations or informal interviews. Ethnographers use this qualitative tool to obtain in a limited amount of time, relevant data that helps produce meaning and an understanding of the phenomenon being studied.

4.10.2.1. Data collection for the Ethnographic inquiry

The researcher used a field diary to record notes about different aspects of the revised intervention during each visit he made to both hospitals between January 2009 and May 2013. Firstly, scratch notes were jotted in the field diary using a few words or short sentences that later helped the researcher to recall what was observed. The scratch notes were then converted into more comprehensive field notes that constituted a coherent and detailed description of the observed phenomenon. Recording of the notes sought to describe the most noteworthy and striking observations made during each visit. Some of the recorded notes were, amongst other things, : the actual setting within which care occurred, the patient-health care interaction, communication channels between the ward and other internal support structures, management support mechanisms, resource (both human and material) mobilisation and staff interactions.

4. 10.2.2 Data analysis for field notes

While there are no standard guidelines in the literature on how to analyse field notes (Burgess, 1991), it was important for the researcher to systematically organise the notes in such a way that they were more perceptible and well aligned to specific themes of inquiry. Field notes were organised to consist of (1) non-verbal notes which described the researcher's impressions / intuitions based on other behavioural cues, and (2) the reflective part, which consisted of direct quotes from opportunistic interviews with the hospital personnel and patients. The non-verbal notes were accompanied by a verbiage which was specific to each impression.

4. 10.3. Data validity and reliability: FGDs

In order to optimise the validity and reliability of the study findings, participants who took part in both categories of focus groups were asked the same questions by the same facilitator. Respondent validation, which is a process that involves cross-checking interim findings, was conducted by means of reflection with participants to ensure that information they had provided had been accurately understood. All the data were also collected and translated by one interviewer thereby minimizing inter-investigator bias (Miles, 1999).

The internal consistency of data coding and analysis processes were maximised by ensuring that the researcher did all the coding and analysis himself. However, a peer reviewing process was undertaken whereby a more senior researcher reviewed the steps taken to analyse as well as interpret the data. This was important to further ameliorate the "inter-rater reliability" of the study findings (Daly, McDonald, Willis,

1992). Furthermore, the focus group material was reviewed by the same senior researcher who understood the study context and was conversant with the conduct of FGDs. This researcher was also present during the discussions to take notes on group dynamics and possible nuances in meaning, opinion and attitude among the participants. The qualitative approach as a whole was appropriate as it provided qualitative meaning to quantitative results (Pope, Mays, 1995) which have been criticised as being mainly concerned with generating results using statistical tests that are based on assumptions (Sandleowski, 2000).

4. 11. Chapter summary

In this chapter, a comprehensive account of research methods used in each phase of the study was given. An operations research approach which consisted of a mixed methods study design, with embedded quantitative and qualitative methodologies, was used to conduct three of the four phases of this study. Phases 2, 3 and 4 involved scientific research methods which were different in nature but complementary in what they were aimed at achieving. The next chapter will present the findings of the study.

CHAPTER 5

STUDY FINDINGS - PART ONE OF PHASE TWO

Epidemiological modelling of the effect of HIV infection, disease stage and other clinical factors on the survival of severely malnourished children

5.1. Chapter introduction

This chapter describes the results of an epidemiological inquiry which sought to compare survival among severely malnourished children with and without HIV infection. Although the main predictors of death reported here are HIV infection and disease stage, the potential effects of other clinical predictors and confounders as well as effect modifiers are also reported. These predictors included case severity on admission and other clinical manifestations on admission which were directly or indirectly related to SAM. Where applicable, results are presented for each hospital separately and compared. However, where statistical analyses showed no between-facility differences, pooled results combining cases from both hospitals are presented.

5.2. Descriptive analyses

The majority of SAM cases admitted throughout the study period and met the study inclusion criteria (50%, n=225) were aged between 13-24 months followed by cases aged 6-12 months (36%, n=165). Cases aged 3-5 years constituted only 14% of the study sample.

Figures 11 (a) through to (f) show the distribution of HIV infection by other clinical characteristics on admission. The slide plots have divergent bars with the HIV positive bar pointed in the negative direction and the HIV negative bar in the positive direction along the x axis. The graphs show that more HIV positive cases were marasmic compared to their HIV negative counterparts, more HIV positive cases had LRTS or other comorbidities compared to their HIV negative counterparts,

and more HIV positive cases were severely ill on admission compared to their HIV negative counterparts.

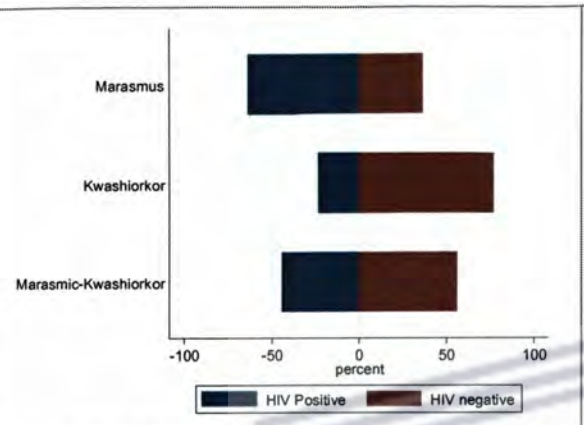

Figure 11.a: *Distribution of HIV infection by SAM syndromic category*

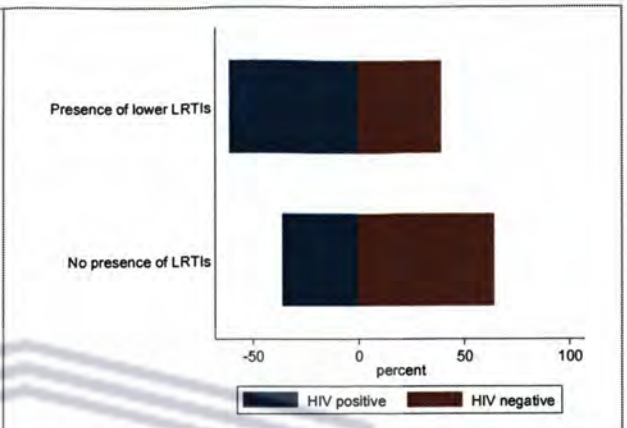

Figure 11.b: *Distribution of HIV infection by presence of LRTIs*

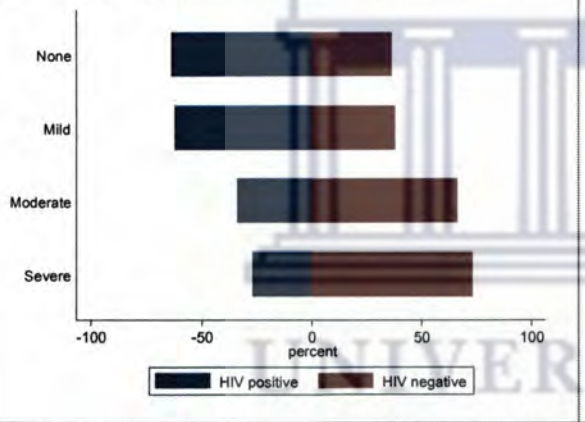

Figure 11.c: *Distribution of HIV infection by oedema grade*

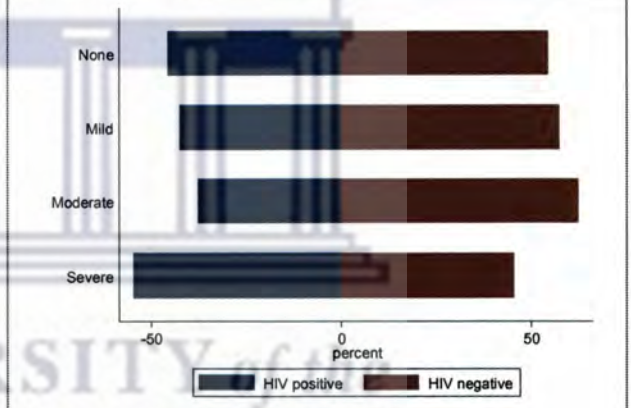

Figure 11.d: *Distribution of HIV infection by dermatosis grade*

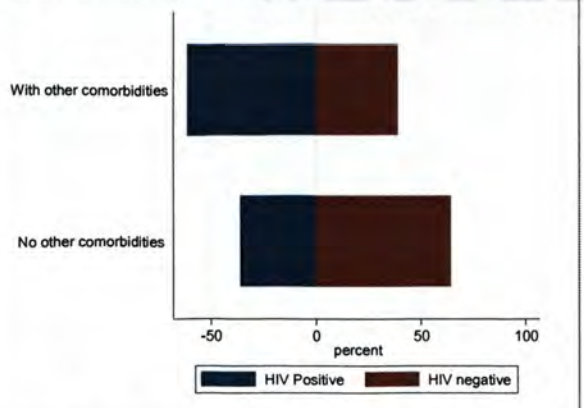

Figure 11.e: *Distribution of HIV infection by presence of other comorbidities*

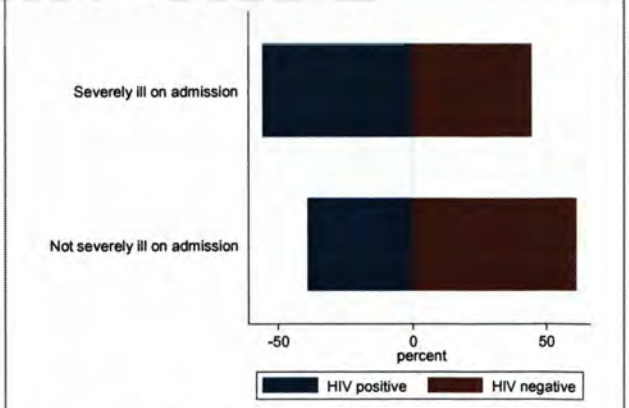

Figure 11.f: *Distribution of HIV infection by severity on admission*

Table 4: Between-hospital comparison of SAM cases by clinical profile on admission:

Variable (*N=454*)	St Patrick's Hospital		Holy Cross Hospital		Both hospitals combined		
	n	(%)#	n	(%)#	n	(%)#	*p*
Severe malnutrition classification							
Marasmus	59	(40.9)	114	(36.8)	173	(38.1)	
Kwashiorkor	61	(42.4)	120	(38.7)	181	(39.9)	
Marasmic - Kwashiorkor	24	(16.7)	76	(24.5)	100	(22.0)	0.17
Oedema grade							
None	52	(36.1)	101	(32.6)	153	(33.7)	
Mild	9	(6.25)	20	(6.45)	29	(6.4)	
Moderate	39	(27.0)	83	(26.7)	122	(26.9)	
Severe	44	(30.6)	106	(34.2)	150	(33.1)	0.85
Dermatosis grade							
None	36	(25.0)	100	(32.6)	136	(29.9)	
Mild	43	(29.8)	63	(20.3)	106	(23.4)	
Moderate	47	(32.6)	110	(35.5)	157	(34.6)	
Severe	18	(12.50)	37	(11.94)	55	(12.1)	0.12
LRTIs							
Yes	48	(33.3)	83	(26.7)	131	(28.9)	
No	96	(66.7)	227	(73.3)	323	(71.2)	0.15
Other comorbidities							
Yes	55	(38.2)	97	(31.3)	152	(33.4)	
No	89	(61.8)	213	(68.7)	302	(66.5)	0.14
Critically ill on admission							
Yes	33	(22.9)	84	(27.1)	117	(25.7)	
No	111	(77.1)	226	(72.9)	337	(74.2)	0.34
HIV status							
Positive	78	(54.1)	118	(38.0)	196	(43.2)	
Negative	66	(45.8)	192	(61.9)	258	(56.8)	0.001
HIV/AIDS disease stage							
Stage 1	18	(23.0)	16	(13.6)	34	(17.4	
Stage 2	22	(28.2)	30	(25.4)	52	(26.5)	
Stage 3	23	(29.4)	50	(42.7)	73	(37.2)	
Stage 4	15	(19.2)	22	(18.6)	37	(18.8)	0.19
Outcome							
Died	34	(24.3)	74	(24.5)	108	(24.4)	
Discharged	106	(75.7)	228	(75.7)	334	(75.6)	0.96

Are column percentages and add up to 100%.

The total number of SAM cases included in the analysis was 454, of which 144 (32%) were from St Patricks Hospital and 310 (68.3%) from Holy Cross Hospital. More cases were obtained from Holy Cross Hospital as the duration of data collection in that facility was much longer compared to St Patricks Hospital. At the latter hospital,

data collection using patient treatment records was stopped after the 32nd month of the study due to internal bureaucratic dynamics.

Table 4 shows the clinical characteristics of study subjects disaggregated by hospital and then combined. The differences between the two hospitals in terms of the distribution of clinical characteristics of SAM cases were, to a large extent, not statistically significant ($p>0.05$). However, this was not the case with regard to HIV status. There were more HIV positive SAM cases than HIV negative at St Patrick's hospital whereas the reverse was true at Holy Cross hospital ($p=0.001$).

When both hospitals were combined, the proportion with Marasmus and Kwashiorkor was similar (38% and 40% respectively) whereas only 22% were classified as Marasmic-kwashiorkor. About a quarter (28%) of SAM cases had LRTIs at admission and a third had other comorbidities, the most common being gastroenteritis. In both hospitals the most commonly diagnosed LRTI was pneumonia. When SAM cases from both hospitals were combined, 196 (43%) were HIV positive and the other 258 (57%) were HIV negative. In total, the majority who tested positive for HIV were at stage 3 of HIV infection (37%) followed by those who were at stage 2 (26.5%), then 19% and 17% for stage 1 and 4 respectively. More SAM cases were at stage 2 and 3 ($n=30$ and $n=50$ respectively) at Holy Cross hospital compared to those at stage 1 ($n=16$) and stage 4 ($n=22$), even though these differences were not statistically significant. At St Patrick's hospital the proportions of cases in each stage were not very different.

About 26% of SAM cases were admitted in a critical condition. The case fatality rate at St Patricks was 24.3% and at Holy Cross it was 24.5%, giving a combined rate of 24.4%.

5.3. Cross tabulations with measures of association

Table 5: Cross tabulation of cases by SAM syndromic classification and HIV status: hospital - specific and pooled analysis (2009 – 2013)

hospital	Clinical classification of Severe Malnutrition								
	Marasmus		Kwashiorkor		Marasmic-Kwashiorkor		Total		[1] *p* value
	n	(%)	n	(%)	n	(%)	n	(%)	
St Patrick's									
HIV Negative	15	22.7	41	62.1	10	15.2	66	100	
HIV Positive	44	56.4	20	25.6	14	17.9	78	100	***p <0.001***
Total	59	40.9	61	42.3	24	16.7	144	100	
Holy Cross									
HIV Negative	48	25.0	98	51.0	46	23.9	192	100	
HIV Positive	66	55.9	22	18.6	30	25.4	118	100	***p <0.001***
Total	114	36.8	120	38.7	76	25.5	310	100	
Both Hospitals combined									
HIV Negative	63	24.4	139	53.8	56	21.7	258	100	
HIV Positive	110	56.1	42	21.4	44	22.5	196	100	***p <0.001***
Total	173	38.1	181	39.9	100	22.3	454	100	

[1] *P-values shown relate to cases with marasmus and Kwashiorkor and all syndromic categories combined. P values for cases with Marasmic-Kwashiorkor (not shown in Table 5) were not statistically significant (i.e. <0.05)*

As shown in Table 5, the differences between cases with regard to syndromic classification and HIV status were all statistically significant, for each hospital and when both hospitals were combined. The pooled analysis showed that more HIV positive SAM cases were marasmic compared to their HIV negative counterparts (about 56% and 24% respectively, $p<0.001$). The reverse was true for cases that had kwashiorkor, where 53% were HIV negative and 21% HIV positive ($p<0.001$). The

same direction of differences was also observed at the level of individual hospitals with a similar statistical significance ($p<0.001$). For cases with marasmic-kwashiorkor there were no statistically significant differences across HIV status.

5.4. Survival analysis

A new variable was created from the existing data on the duration of hospitalisation so that cases that died could be isolated. This was done so that the mean duration from admission to death could be computed for each hospital. The analysis showed that children who were admitted at St Patricks hospital with SAM and died stayed, on average, 7.5 days in the hospital before they died (Mean duration = 7.5; SE = 1.12; 95% CI = 5.09 - 9.96). At Holy Cross hospital, the average time from admission to death was 5 days (Mean=5.8; SE = 0.59; 95% CI = 3.9 - 6.25). The difference between the two hospital was statistically significant (Mean difference = 2.44; SE=1.18; 95% CI = 0.09 -4.81; p = <0.05).

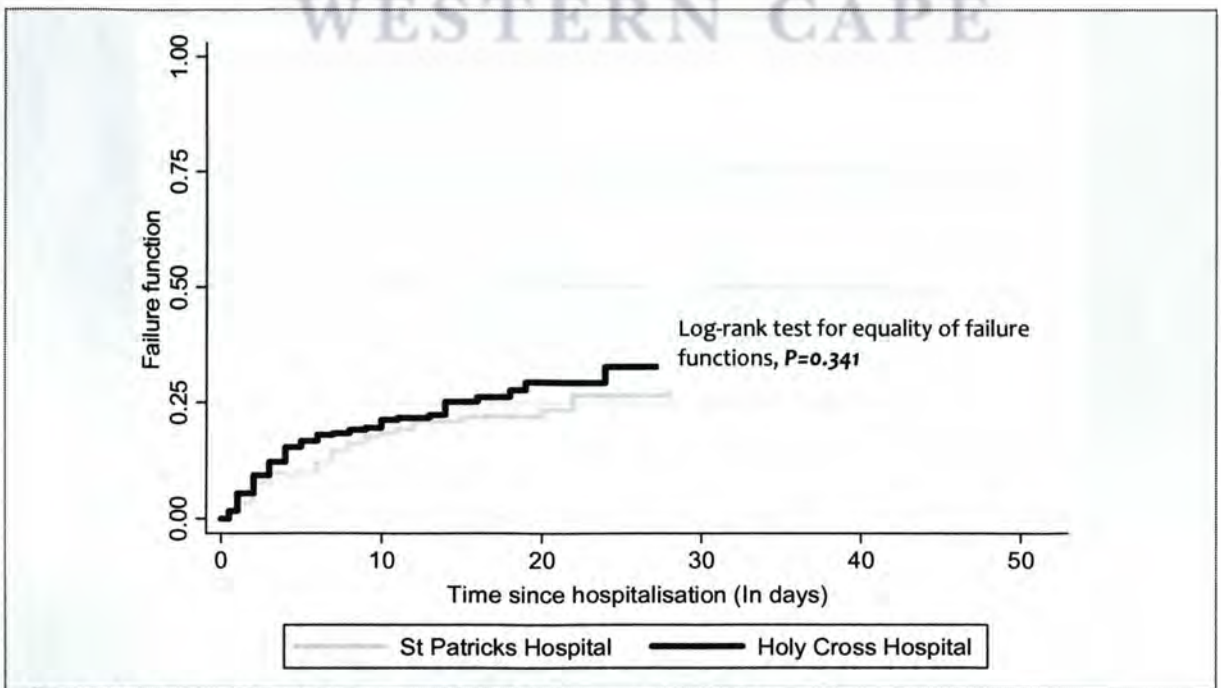

Figure 12: *Kaplan-Meier failure curves for SAM cases stratified by hospital*

Figure 12 compares estimates of unadjusted hospital-level survival prospects for SAM cases regardless of their HIV status. As shown in the figure, the hospital to which children were admitted during the study period was not a risk for mortality. Even though mortality at Holy Cross Hospital was slightly higher than St Patrick's Hospital, this difference was not statistically significant (p=0.341). As will be shown later in Chapter 7, however, temporal analysis of mortality trends revealed differences in mortality between the two facilities over the study period.

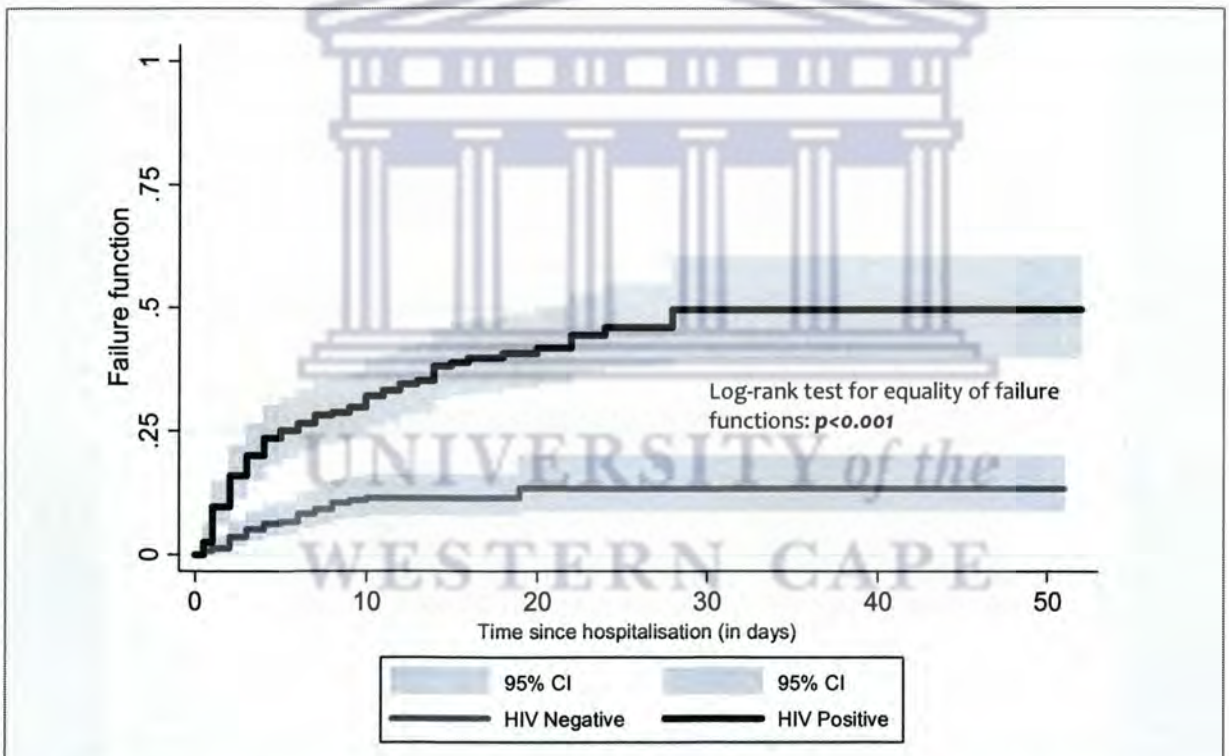

Figure 13: *Kaplan-Meier failure curves for SAM cases stratified by HIV status: Pooled analysis*

The cross-tabulation analysis revealed that 41.15% of HIV positive and 11.6% of HIV negative SAM cases died while on treatment (p=<0.0001). Figure 13 above compares failure (death) curves between HIV positive and negative SAM cases admitted during the study period (2009 - 2013), regardless of the hospital from which they were recruited. HIV positive cases had worse survival prospects than their HIV

negative counterparts in both hospitals. This unadjusted difference was statistically significant (log-rank test $p < 0.001$). As shown in the graph, the cumulative fraction of the original group of HIV positive SAM cases who had died on Day 6 was 25% compared to the cumulative fraction of HIV negative cases which was about 5% at the same time point. The failure curve for HIV positive SAM cases levels out later at Day 28 when about 50% of the 40% that died had died, whereas the failure curve of HIV negative cases plateaus at Day 10 when only about 12% of HIV negative cases had died. These results imply that HIV positive cases generally died sooner and in greater numbers following admission, than their HIV negative counterparts.

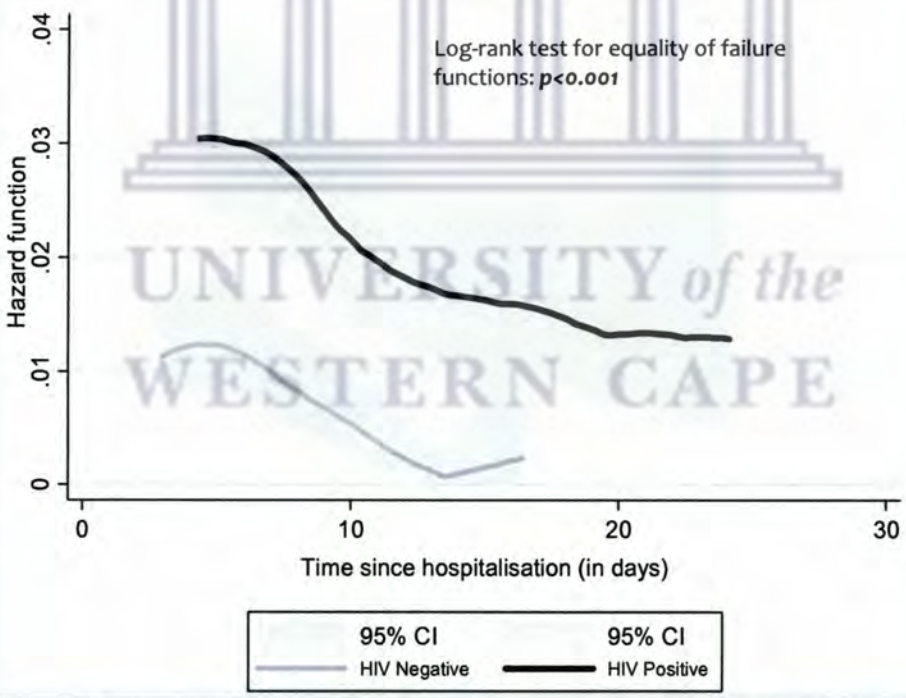

Figure 14: *Smoothed hazard curves for SAM cases stratified by HIV status – Pooled analysis*

Figure 14 complements the graph presented in Figure 13. Generally, the mortality hazard was consistently higher for HIV positive cases than HIV negative cases at any time since hospitalisation. Also, there was a higher risk in the period just after

admission for both groups which then subsequently declined during the treatment period.

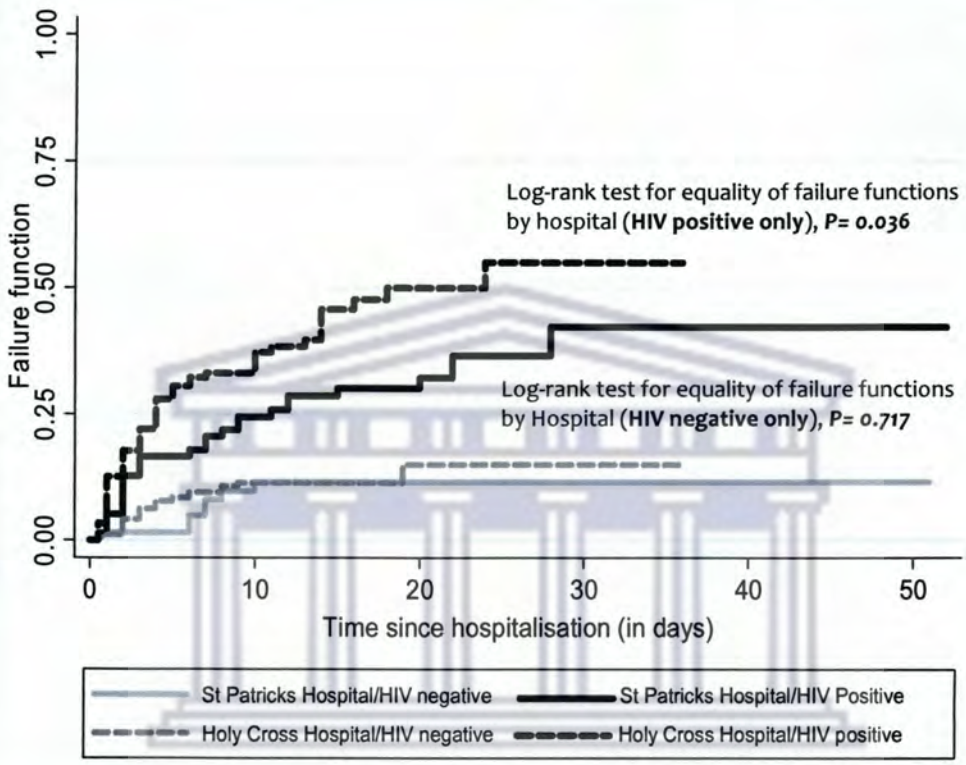

Figure 15: *Kaplan-Meier failure curves for SAM cases stratified by HIV status and hospital*

Although it was shown earlier in Figure 12 that the hospital to which SAM cases were admitted was not a risk for mortality, this was not the case when HIV status was considered. In Figure 15, the risk of death was higher at Holy Cross hospital than St Patrick's hospital for HIV positive SAM cases (p= 0.036). Conversely, there was no statistically significant difference in risk of death between the hospitals for HIV negative SAM cases (p= 0.717).

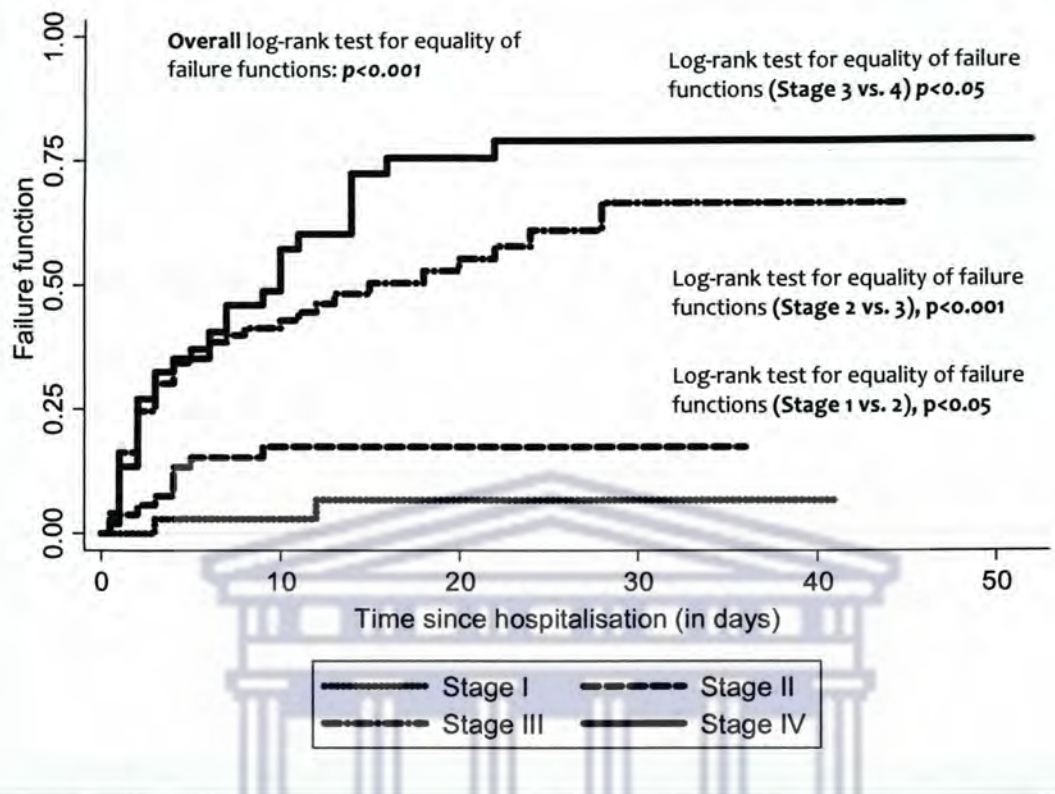

Figure 16: *Kaplan-Meier failure curves for SAM cases stratified by HIV clinical stage - Pooled analysis*

Figure 16 compares unadjusted failure curves for HIV positive AM cases admitted with different HIV clinical stages. Generally, children who were at Stage 4 of HIV infection had significantly worst survival prospects followed by those who were at Stage 3. The difference between these two groups was statistically significant ($p<0.05$). Although survival prospects among cases that were at Stage 1 were better than those at Stage 2, the difference was statistically marginal ($p=0.04$). However, survival prospects between HIV positive cases who were at Stage 2 and those who were at Stage 3 were highly significant ($p<0.001$).

Figure 16 also shows that the cumulative fraction of SAM cases at Stage 3 who had died by Day 3 was 25% compared to that of SAM cases who were at Stage 2 and 1 (1% and 0% respectively at the same time point). Also, the failure curves for SAM

cases at Stage 2 levelled out sooner at Day 5 when about 15% of the cohort had died, whereas the failure curve for cases at Stage 3 only plateaus at Day 28 when about 65% had died. This may imply that the critical stage for higher risk of death is when cases are admitted at Stage 3, followed by Stage 4.

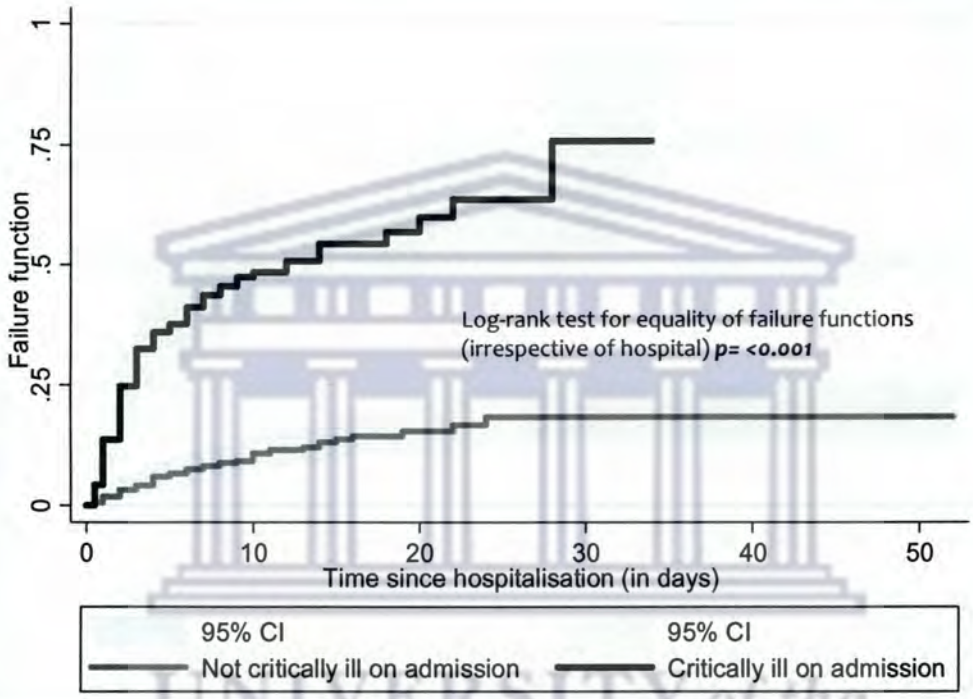

Figure 17: *Kaplan-Meier failure curves comparing SAM cases who were critically ill on admission and those who were not - Pooled analysis*

A comparison was made between SAM children who were critically ill on admission and those who were not. The analysis focused on aggregated data from both hospitals. As shown in the figure, about 25% of children admitted in a critical condition had died by the second day. Only 1% of the non-critically ill group had died by the second day of hospitalisation. Mortality patterns beyond the second day showed that about 75% of critically ill children with SAM had died by the 28th day of hospitalisation compared to about 17% who were not critically ill. On aggregate, the

difference in these unadjusted estimates of survival between the two groups was highly statistically significant ($p<0.001$).

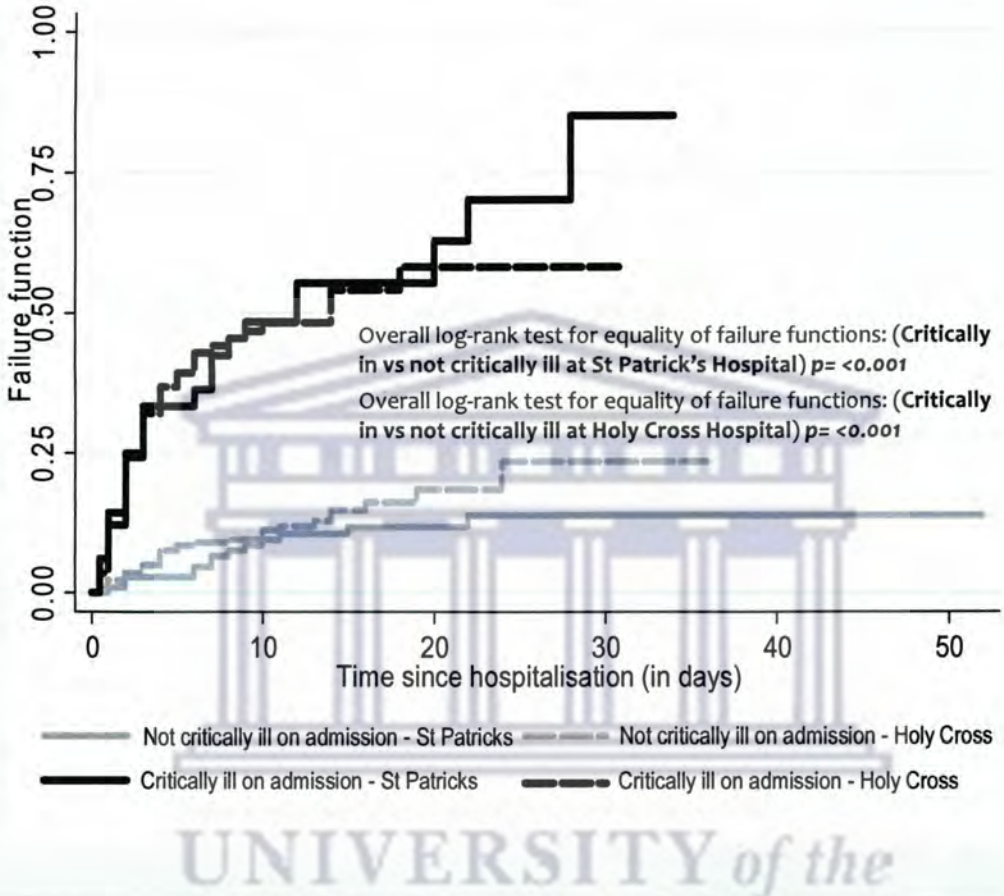

Figure 18: *Kaplan-Meier failure curves comparing SAM cases who were critically ill on admission and those who were not– Hospital level analysis*

Unadjusted estimates of failure were also generated to compare children admitted with SAM who were critically ill on admission and those who were not within each hospital. Figure 18 shows that in both hospitals, the probability of failure was higher among critically ill cases than in cases that were not critically ill cases. There was no difference between the two hospitals. This result mirrors what was reported in Figure 17 when data from both hospitals were aggregated.

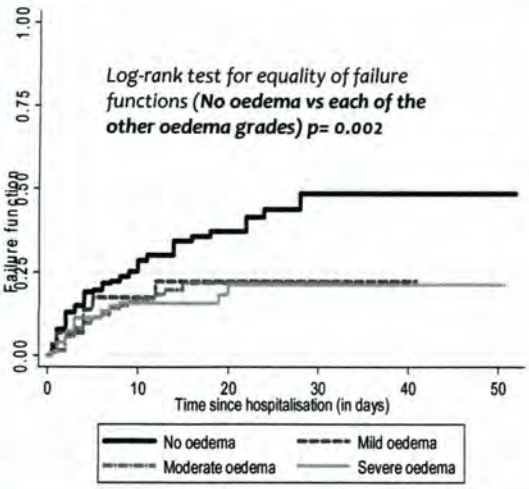

Figure 19 (a): *Kaplan-Meier failure curves for SAM cases stratified by oedema grade - Pooled analysis*

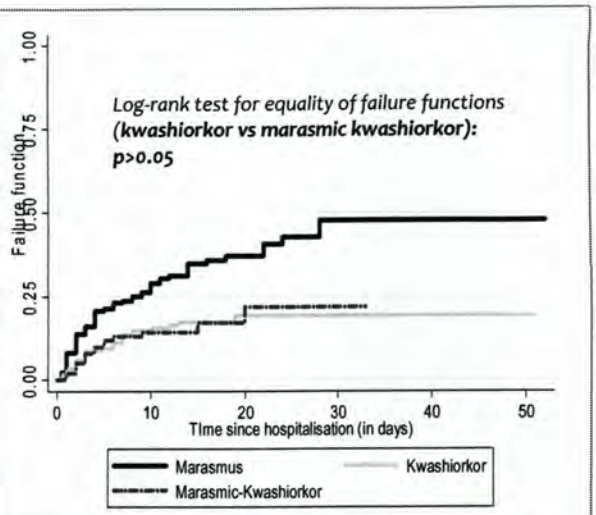

Figure 19 (b): *Kaplan-Meier failure curves for SAM cases stratified by syndromic manifestation – Pooled analysis*

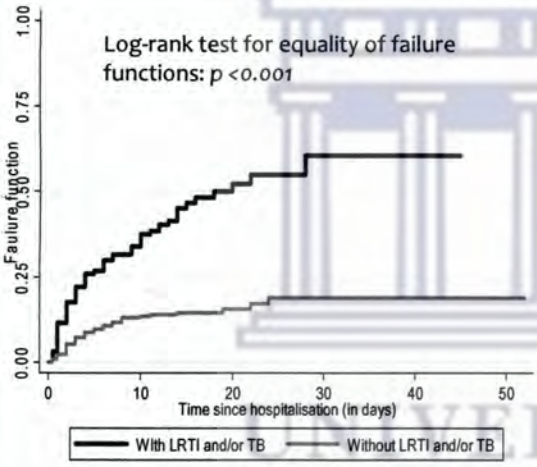

Figure 19 (c): *Kaplan-Meier failure curves for SAM cases stratified by presence of LRTIs - Pooled analysis*

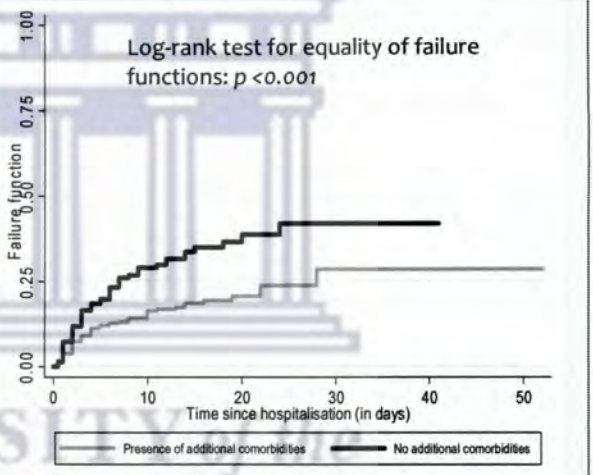

Figure 19 (d): *Kaplan-Meier failure curves for SAM cases stratified by presence of other comorbidities - Pooled analysis*

Figures 19 (a), (b), (c) and (d) show the comparisons of unadjusted failure curves for SAM cases by comorbidities other than HIV infection. The failure rate of SAM cases that had no oedema was higher compared to the failure rate of those who had other grades of oedema (p=0.01). This finding supports the results obtained when SAM cases were compared based on the SAM syndromic manifestations on admission. Marasmic cases that had no oedema had the worst survival prospects compared to kwashiorkor or marasmic-kwashiorkor cases. Interestingly, there were no

statistically significant differences between cases that had mild, moderate and severe oedema, in terms of failure rates ($p>0.05$). No differences were also found between cases that had Kwashiorkor and marasmic kwashiorkor ($p>0.05$). Furthermore, the presence of other comorbidities was associated with poorer survival, as was the case for co-infection with LTRIs / TB ($p<0.001$).

Table 6: *Descriptive analysis of quality of clinical care indicators: Pooled analysis*

Thematic indicators of quality of care	n	Median	[IQR]	Min	Max	IEP [a,b]
Score for treatment and prevention of hypoglycaemia	454	13	[12-14]	5	14	[0,14]
Score for treatment of infection	454	4	[4-4]	1	4	[0,4]
Score for electrolyte imbalance & micronutrient deficiency	454	12	[11-13]	2	13	[0,13]
Score for management of rehydration	404	11	[10-11]	1	11	[0,11]
Score for treatment of shock	140	4	[2-4]	0	4	[0,4]
Score for blood transfusion	75	3	[2-3]	0	3	[0,3]
Score for patient monitoring	450	4	[4-4]	0	4	[0,4]
Score for appropriate patient discharge procedure	334	6	[5-6]	0	7	[0,7]

SD=standard deviation; IEP = Interval End Points for the score on each quality of care indicator; IQR = interquartile range

Table 6 provides descriptive summaries of scores for different thematic indicators of care quality using aggregated data collected during the period 2009 to 2013 from both hospitals. As explained in Chapter 4, the score for each thematic indicator was generated based on several interrelated sub-indicators which represent the WHO 10 step guidelines. The interval end-points [a,b] in Table 6 show the range of scores allocated to each thematic indicator, whereby "b" represents the highest score achievable for that indicator and "a" the lowest.

The median scores and the corresponding interquartile ranges for quality-of-care indicators were comparable to the maximum scores achievable. Also worth mentioning is the fact that not all quality-of-care indicators were evaluated for all the SAM cases. This is because some cases did not require all the treatment procedures, and hence the uneven distribution of observations (n) across all thematic indicators shown in Table 6 and 7. Table 6 also shows that there were more SAM cases treated for shock and those who received blood transfusion than would be expected, indicating possible mismanagement of cases

Table 7: *Descriptive comparison of quality of clinical care indicators between the two hospitals: hospital-level analysis (2009 – 2013)*

Thematic indicators of quality of care	Hospital	n	Median	Min	Max	IEP [a,b]
Score for treatment of hypoglycaemia	***Holy Cross***	144	12	6	14	
	St Patricks	310	13	5	14	[0,14]
Score for treatment of infection	***Holy Cross***	144	3	1	4	
	St Patricks	310	4	2	4	[0,4]
Score for electrolyte imbalance & micronutrient deficiency	***Holy Cross***	144	10	2	13	
	St Patricks	310	11	5	13	[0,13]
Score for management of rehydration	***Holy Cross***	132	10	2	11	
	St Patricks	272	11	1	11	[0,11]
Score for treatment of shock	***Holy Cross***	47	3	0	4	
	St Patricks	93	3	0	4	[0,4]
Score for blood transfusion	***Holy Cross***	26	3	0	4	
	St Patricks	49	3	0	13	[0,13]
Score for patient monitoring	***Holy Cross***	144	3	0	4	
	St Patricks	306	4	1	4	[0,4]
Score for appropriate patient discharge procedure	***Holy Cross***	107	6	0	7	
	St Patricks	227	7	0	7	[0,7]

SD=standard deviation; IEP = Interval End Points for the score on each quality of care indicator

Comparison of quality of care between the two hospitals based on mean scores revealed that generally St Patrick's hospital scored better on all thematic indicators

of quality of care than Holy Cross hospital as shown in Table 7. This finding may help explain the slight differences in treatment outcomes between the two hospitals in terms of survival prospects of SAM cases that had various comorbidities, as well as the rate of weight gain and duration of hospitalisation as will be shown in the next chapter. However, this pattern of results only applies to the period during which the intervention was active. Chapter 7 shows the changes in some outcomes which reflect possible concomitant changes in the quality of care following the discontinuation of the intervention.

Table 8: Univariate *and adjusted Multivariate Cox non-parametric proportional hazard models for factors associated with mortality among children with SAM admitted to St Patricks and Holy Cross hospitals during the intervention period: Pooled analysis*

Factors	Statistic								
		Unadjusted Model				Adjusted Model [ii, iii]			
	n/N*	HR**	95% CI		p	HR***	95% CI		p
			[Lower]	[Upper]			[Lower]	[Upper]	
Hospital									
St Patrick's	34/140	1							
Holy Cross	74/302	1.22	0.81	1.84	>0.05	—	—	—	—
Age									
6-12 months	47/159	1				1			
13-24 months	47/222	0.73	0.48	1.09	>0.05				
25-36 months	12/40	1.03	0.55	1.95	>0.05				
37-60months	2/21	0.15	0.21	1.05	>0.05				
SAM Classification									
Marasmus	63/173	1				1			
Kwashiorkor	30/171	0.44	0.29	0.69	**<0.001**	1.21	0.42	3.45	>0.05
M-Kwashiorkor	16/98	0.44	0.25	0.77	**<0.001**	0.53	0.20	1.43	>0.05
Oedema grade									
None	54/153	1				1			
Mild	6/29	0.55	0.24	1.29	>0.05	0.58	0.22	1.53	>0.05
Moderate	23/119	0.52	0.31	0.84	**<0.01**	1.16	0.43	3.07	>0.05
Severe	29/141	0.46	0.29	0.74	**<0.01**	0.61	0.20	1.83	>0.05
Dermatosis grade									
None	32/134	1				1			
Mild	23/102	0.88	0.52	1.51	>0.05	0.69	0.37	1.26	>0.05
Moderate	33/153	0.90	0.56	1.47	>0.05	1.03	0.59	1.80	>0.05
Severe	20/53	1.73	0.10	1.04	=0.05	1.43	0.76	2.66	>0.05
LRTIs and/or TB									
No	47/314	1				1			
Yes	61/128	3.66	2.50	5.36	**<0.001**	1.74	1.12	2.70	**<0.01**
Other comorbidities									
No	56/294	1				1			
Yes	52/148	1.94	1.33	2.84	**<0.001**	1.14	0.74	1.76	>0.05
Critically ill on admission									
No	44/328	1				1			
Yes	64/114	5.70	3.87	8.39	**<0.001**	3.64	2.35	5.64	**<0.001**
HIV Status & Stage									
Negative	29/250	1				1			
Positive/Stage I	2/33	0.46	0.11	1.94	>0.05	0.20	0.03	1.53	>0.05
Positive/Stage II	9.50	1.44	0.68	3.05	>0.05	1.12	0.51	2.49	>0.05
Positive/Stage III	40/72	5.73	3.54	9.25	**<0.001**	3.18	1.85	5.47	**<0.001**
Positive/Stage IV	28/37	8.12	4.82	13.66	**<0.001**	3.74	2.05	6.84	**<0.001**

- *n/N*: Number of failure cases over total number of cases*
- *HR**: Unadjusted Hazard Ratio*
- *HR***: Adjusted Hazard Ratio*
- *p: level of significance*
- *1: represents the reference category*

The univariate and multivariate Cox non-proportional hazard models shown in table 8 are based on pooled data collected from both hospitals from January 2009 to May

2013. The models identify significant predictors and confounders of mortality for SAM cases. The unadjusted model revealed that hospital was not a statistically significant predictor of mortality (p=0.35), a finding also reported in Figure 12 about case failure rates between the two hospitals. Also, age was not a statistically significant predictor of mortality both in the unadjusted and adjusted models (p>0.05), probably because of a small number of older children in the cohort

At univariate level, children who were admitted with Kwashiorkor and Marasmic Kwashiorkor had a 56% lower hazard of dying compared to those who had Marasmus (p<o.o1). However, after adjusting for other potential confounders, these differences were not statistically significant (p>0.05). For severely malnourished children who had severe oedema, the hazard of death was 46% less than the hazard of dying among those who had no oedema (p<o.o1). For cases with moderate oedema the hazard of death was 48% lower (p<o.o1) and those mild oedema 45% lower (p>o.o5). After adjusting for other factors, none of the oedema grades was a statistically significant predictor of mortality (p>0.05). The same pattern was observed for the different dermatosis grades which were not statistically significant predictors of mortality (p>0.05) after model adjustment. However, at univariate level severe dermatosis was associated with 70% higher hazard of death compared to no dermatosis but this was not statistically significant (p=o.o5).

Before risk factor adjustment, severely malnourished children who had either LRTI's and/or TB had about 4 times higher hazard of death compared to those who did not (HR=3.77, p<o.o1). However, the hazard level was reduced after multivariate adjustment (HR=1.74, p<o.o5). Cases admitted with other comorbidities had almost a

two-fold higher hazard of death than those admitted without (HR=1.94, p<o.o1). The size of the hazard was slightly smaller after adjusting for other factors but nevertheless not statistically significant (HR=1.41, p>o.o5).

The HIV status and case severity were the strongest predictors of death both in the unadjusted and adjusted models. The unadjusted model revealed that children who were critically ill on admission had a five times higher hazard of death than those who were not (HR=5.70, p<o.o1). However, after adjusting for other factors, the hazard dropped a little but remained statistically significant (HR=3.64, p<o.0o1). Severely malnourished children who were HIV positive and at Stage 4 and 3 of infection had, respectively, an eight times higher (HR=8.12, p<o.o01) and five times (HR=5.73, p<o.o01) higher hazard of death, than their HIV negative counterparts. After multivariate adjustment, however, the hazard ratios dropped to about three times for both stages but remained statistically significant (p<o.o01). This implies that other factors confounded the magnitude of risk when the model was adjusted. At both univariate and multivariate levels, Stage 2 and 1 of HIV infection were not statistically significant predictors of mortality (p>o.o5).

With regard to the weighted quality of clinical care score, for every one unit increase in the composite score of quality of care, the hazard of death decreased by 34% (ß=0.66; CI [0.59-0.73]; p<0.01) in the unadjusted model but dropped to 24% (ß=0.72; CI [0.67-0.87]; p<0.001) in the adjusted model.

The Global test for hazard proportionality revealed that the overall model did not significantly violate the proportional hazards assumption (*P-value*=0.184). Overall,

the Variance Inflation Factor (VIF) for the model was 2.87 i.e. <10. The general rule of thumb is that a VIF≥10 (≥5) suggests significant co-linearity between covariates which would affect coefficient estimation.

5.5. Interaction modelling

Table 9: *Cox Non-parametric Proportional Hazard Model for interaction of factors associated with mortality among children with SAM admitted to both hospitals during the intervention period*

Interaction terms					Statistics		
			n*/N	HR#	95% CI		p
HIV (0=No, 1=Yes)	LRTI/TB (0=No, 1=Yes)	Critically Ill on admission (0=No, 1=Yes)			[Lower]	[Upper]	
			9/165	1			
0	0	1	9/35	4.83	1.92	12.18	**<0.001**
0	1	0	3/35	1.55	0.42	5.71	>0.05
0	1	1	8/15	14.64	5.64	38.01	**<0.001**
1	0	0	12/89	2.18	0.92	5.19	>0.05
1	0	1	17/25	22.00	9.78	49.49	**<0.001**
1	1	0	20/39	9.86	4.49	21.68	**<0.001**
1	1	1	30/39	19.79	9.39	41.73	**<0.001**

Modelling of potential interactions (synergies) between factors identified in the multivariate adjusted model as significant predictors of mortality was also done. The reference group during this analysis was SAM cases who were not exposed to any of the 3 factors in the interaction model. As shown in Table 9, cases who had LRTI's/TB and were critically ill at admission had 14 times higher hazard of death compared to those who had none (p<o.o01). Furthermore, children who were HIV positive and critically ill on admission had the highest hazard of death (HR=22, p<o.o01) compared to those who were not exposed to any of the three risk factors. SAM cases

who were HIV positive and had LRTI's / TB, had only 9 times higher hazard of death (p<o.o01).

The hazard of death for HIV infection alone, however, was only 2 times higher than not having any of the three factors. On the other hand, the hazards of being critically ill on admission and having LRTI's / TB were, singly, 4 and 1 times higher, respectively. This may imply that being critically ill and having LRTI's / TB were, both individually and as a combination, potential effect modifiers of risk as they increased the hazard of death quite substantially when they were combined with HIV infection in the interaction model.

Interestingly, the hazard of death was slightly lower (HR=19, p<o.o01) for cases that were HIV positive, had LRTI's and were critically ill on admission compared to those who only had HIV infection and were critically ill on admission (HR=22, p<o.o01) but not so different if you consider the 95% confidence intervals.

In comparison to cases that had none of the risk factors, those who were exposed to only one of the three risk factors had lower hazards of death than those who were exposed to more than one. The predictive power of one risk factor during interaction analysis was generally not statistically significant (p>o.o5) except for critical illness (p=o.o01).

5.6. Time of death analyses

Time of death analysis was also carried out to identify specific times of the day during which SAM cases died. Results from this analysis are shown in Figure 20 and 21 below.

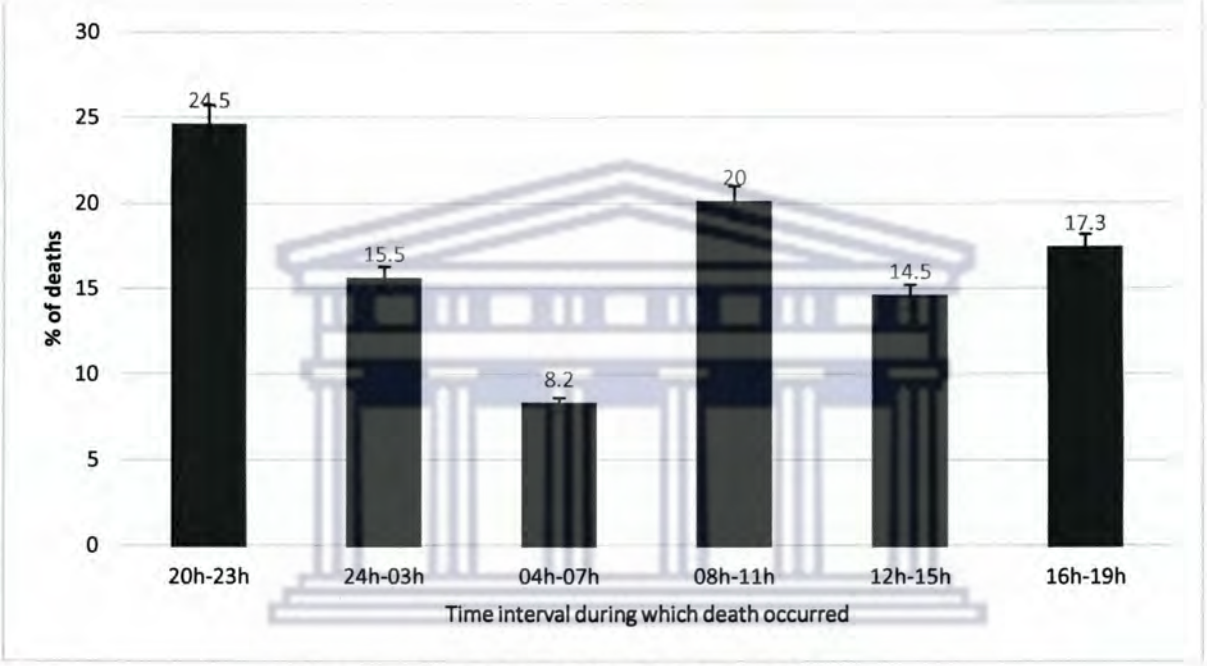

Figure 20: *Distribution of SAM case fatalities by time of death – pooled analysis from both hospitals (2009 - 2013)*

When data from all hospitals were combined, most cases (24.5%) died between 20h and 23h, followed by the period between 08h00 and 11h00 and lastly 16h00 to 190hoo (Figure 20). However, when data were disaggregated by hospital, there were some differences in time intervals during which most SAM deaths occurred. Overall, most deaths occurred between 17h in the evening and 08h in the morning. As shown in Figure 21 below, about 64% of SAM cases at Holy Cross Hospital died after regular working hours (28.4% between 20h00 - 23h00, 21.6% between 24h00 and

03h00, 2.3% between 04h00 and 08h00 and 13.53% between 17h00 and 20h00). The same pattern was also observed at St Patrick's hospital where about 62% of SAM cases also died after regular working hours (16.7% between 20h00 - 23h00, 2.81% between 24h00 and 03h00, 19.40% between 04h00 and 08h00 and 25% between 17h00 and 19h00).

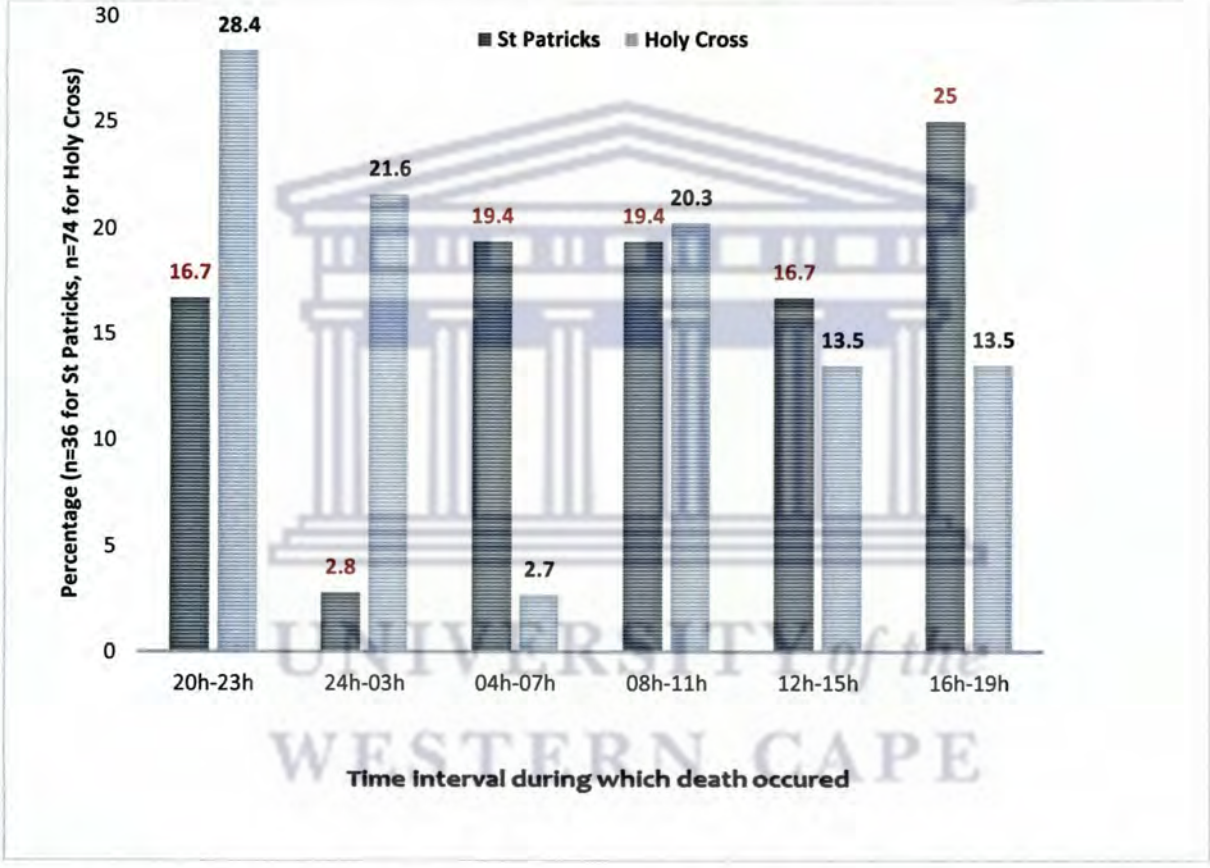

Figure 21: *Distribution of severe malnutrition case fatalities by time of death – Individual hospital analysis (2009 -2013)*

5.7. Chapter summary

In this chapter, the results from the first part of Phase 2 of the study were presented to answer the pertinent research questions. Data analyses revealed that the CFR was higher among HIV positive SAM cases than HIV negative ones, implying worse survival prospects among HIV infected SAM cases. Compared to earlier stages of

HIV infection, survival was poorer for HIV positive SAM cases that were at stage 3 and 4 at admission. The risk of death was highest for Stages 3 and 4 of HIV infection.

The Cox regression showed that although a wide range of factors were associated with death, HIV status and case severity at admission were the strongest independent predictors of death among SAM cases, both in the adjusted and unadjusted models. This was also true when both predictors were combined in the interaction model. Being critically ill and having LRTI's were, both independently and as a combination, potential effect modifiers of higher risk of death as they increased the hazard of death quite substantially when they were combined with HIV infection in the interaction model.

Generally there were no significant differences between the two study hospitals in terms of the patterns of survival and clinical manifestations among SAM cases who were admitted. However, with regard to the quality of clinical care, St Patrick's hospital scored better on a number of indicators of quality of care than Holy Cross Hospital.

The next chapter will present findings from the second part of Phase two which focused on the rate of weight gain and duration of hospitalisation among children with SAM, also in the context of HIV infection.

CHAPTER 6

STUDY FINDINGS - PART TWO OF PHASE TWO

Duration of hospitalisation and the rate of weight gain in severely malnourished children with and without HIV infection

6.1 Chapter introduction

This chapter presents the findings related to nutritional recovery (defined as the rate of weight gain) and duration of hospitalisation. In particular, the relationship between nutritional recovery and duration of hospitalisation in the context of HIV infection is demonstrated. This analysis was of particular interest to the researcher as it has policy implications. As will be discussed in Chapter 8, duration of hospitalisation did not necessarily depend on nutritional or clinical recovery of the patient. Other contextual factors at facility level were at play in both hospitals. Predicting how long an HIV positive SAM case needed to stay in the hospital to achieve a target weight compared to an HIV negative case was therefore necessary to inform policy changes at hospital level.

6.2. Rate of weight gain and clinical manifestations

The rate of weight gain was estimated based on the post-stabilisation period of SAM management.

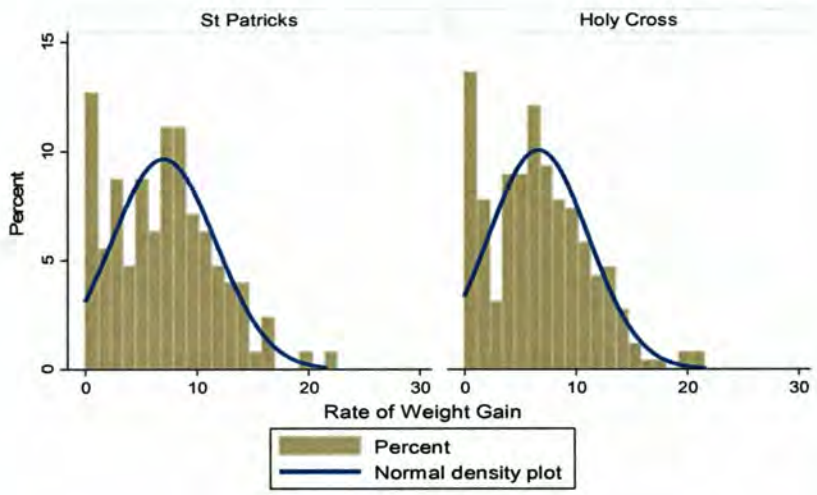

Figure 22.a: *Distribution of the rate of weight gain by hospital*

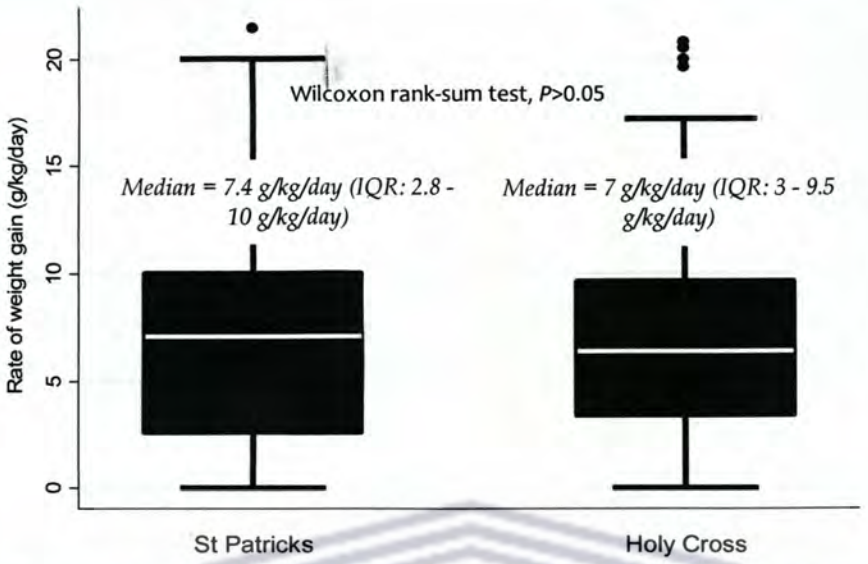

Figure 22. b: *Between-hospital comparison of the rate of weight gain regardless of HIV status: Analysis of discharged cases (2009 - 2013)*

The Mann – Whitney U test revealed no statistically significant difference in the rate of weight gain between St Patrick's Hospital (n=144) and Holy Cross hospital (n=310) when the HIV status or disease stages were not considered ($\boldsymbol{U}$= 10324; $\boldsymbol{Z}$= 5.454; $\boldsymbol{p}$= >00.05). As shown in Figure 22.b, the median rate of weight gain for St Patrick's hospital was almost similar to that for Holy Cross Hospital (7.40 and 7.00 g/kg/day, respectively). The magnitude of the corresponding interquartile ranges was also similar.

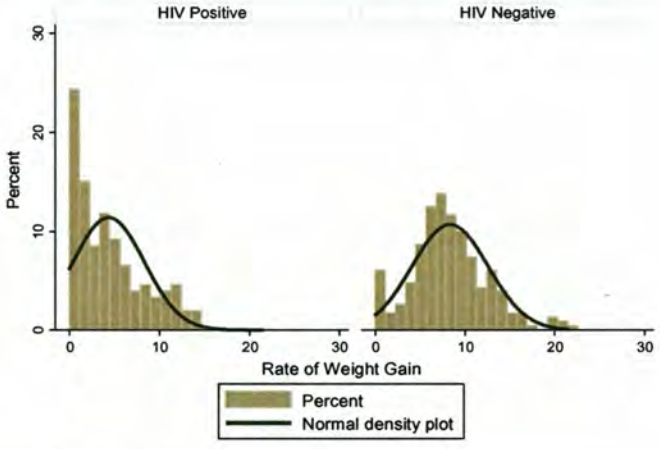

Figure 23.a : *Distribution of rate of weight gain by HIV status*

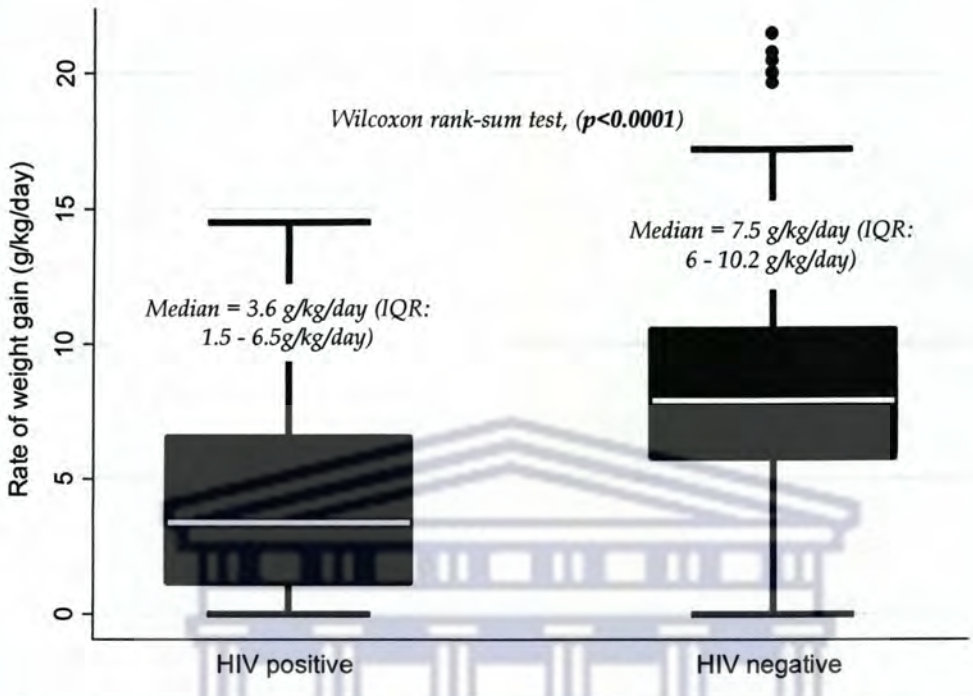

Figure 23. b: *Distribution of rate of weight gain by HIV status: Pooled analysis of discharged cases (2009 - 2013)*

Figure 23.b compares HIV positive and HIV negative SAM cases in terms of the rate of weight gain using aggregated data from both hospitals. The results from the Wilcoxon rank-sum test showed that rate of weight gain for HIV positive SAM cases was poorer (Median=3.6g/kg/day) than that of HIV negative SAM cases (Median=7.5/kg/day). This difference was highly statistically significant (p<0.0001). There were five outliers among the HIV negative SAM cases whose rate of weight gain ranged between 19 and 24 g/kg/day. However, these outliers were not included during the computation of medians. This was probably a result of measurement bias

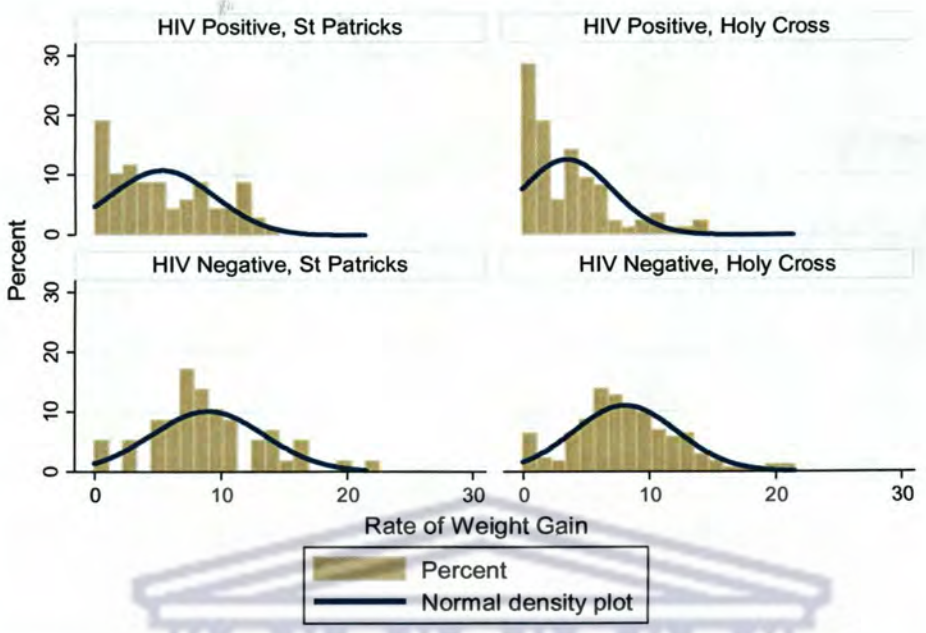

Figure 24. a: *Distribution of rate of weight gain by HIV status, disaggregated by hospital*

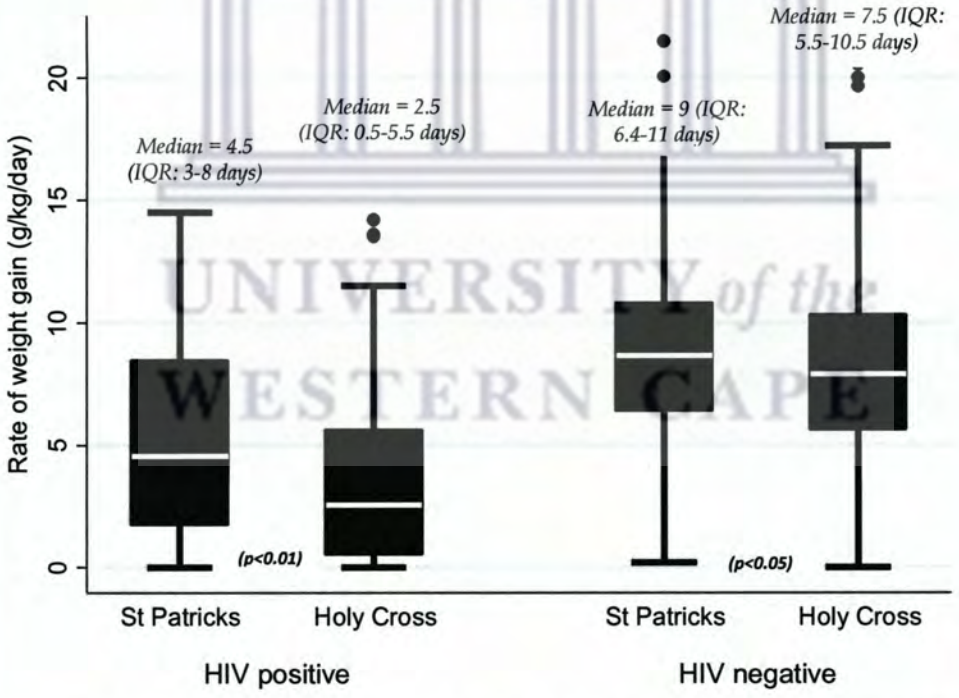

Figure 24.b: *Distribution of rate of weight gain by HIV status: hospital level analysis of discharged cases (2009 -2013)*

When data were disaggregated by hospital, the same pattern was observed (see Figure 24.b). *Within* each hospital, the median rate of weight gain was higher for HIV negative SAM cases than HIV positive ones. However, St Patrick's hospital recorded

better rates of weight gain than Holy Cross hospital among both HIV positive and negative cases. The median rate of weight gain among HIV positive SAM cases was 4.5 g/kg/day at St Patrick's hospital versus 2.5 g/kg/day at Holy Cross hospital. With regard to HIV negative SAM cases, the median rate of weight gain was 9 g/kg/day at St Patrick's hospital versus 7.5 g/kg/day at Holy Cross hospital.

Post-hoc analysis using non-parametric tests were used to compute multiple comparisons of the two hospitals based on the HIV status and the rate of weight gain also revealed that these differences were statistically significant (p value ranged between <o.o01 and <0.05).

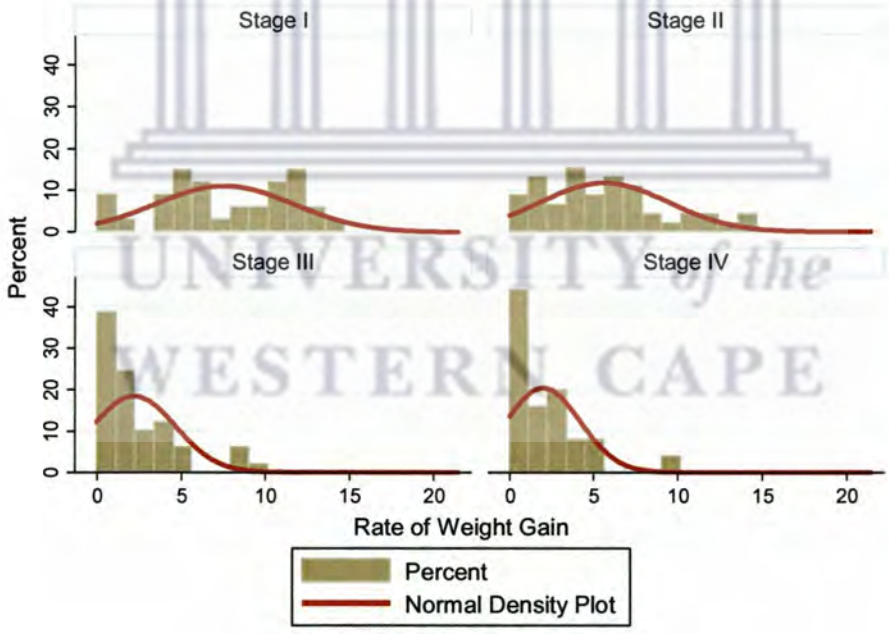

Figure 25.a: *Distribution of rate of weight gain by HIV disease stage*

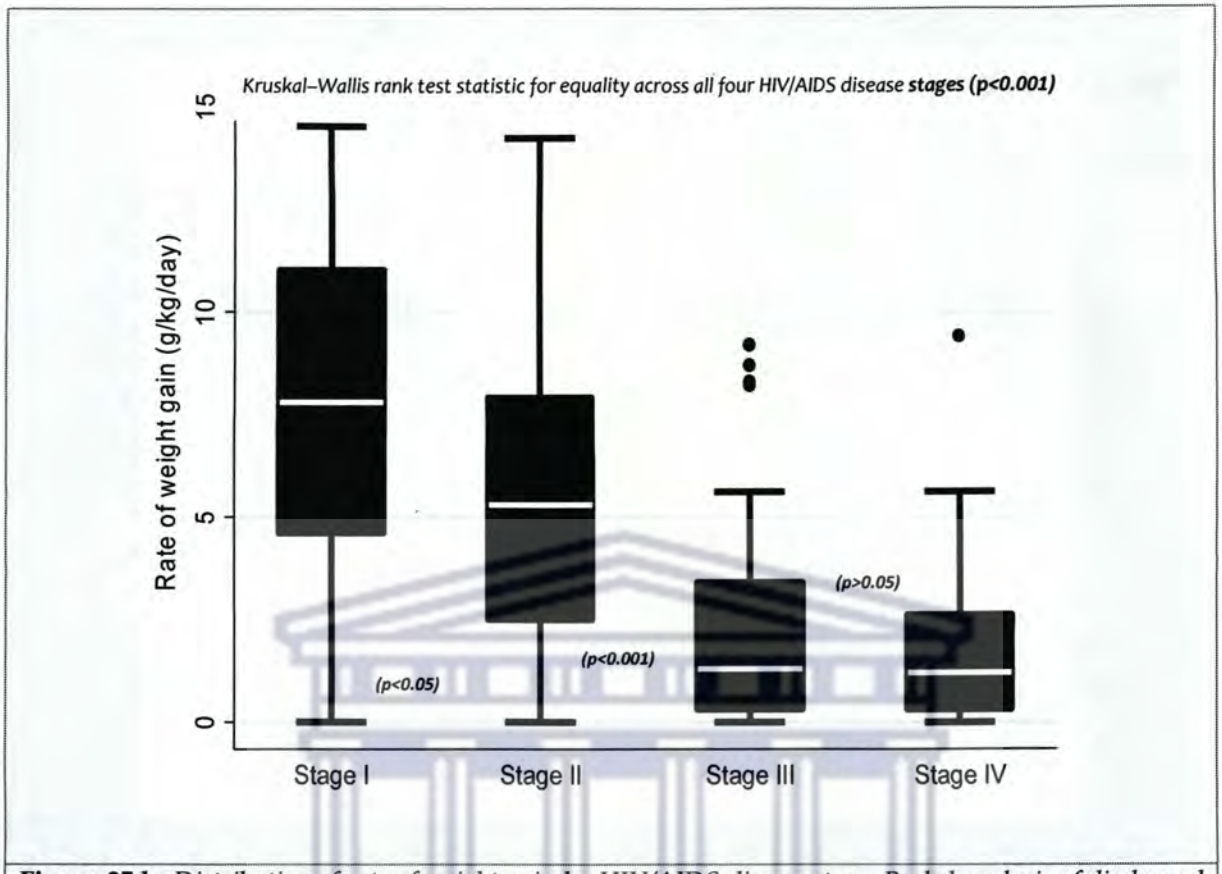

Figure 25.b: *Distribution of rate of weight gain by HIV/AIDS disease stage: Pooled analysis of discharged cases (2009 -2013)*

The two-sample Wilcoxon rank-sum test was used to compare various pairs of HIV disease stages with regards to the rate of weight gain using aggregated data from both hospitals. As depicted in Figure 25.b, the test revealed a statistically significant difference in the rate of weight gain between Stages 1 (n=33; Median= 8g/kg/day) and 2 (n=45; Median=5.2 g/kg/day), p=0.039. A statistically significant difference was also found between Stages 2 (n=45) and 3 (n=49; Median= 1.5g/kg/day), P= <0.001. However, no statistically significant difference was found between stages III (n=49) and IV (n=34), P= 0.841. Both groups had the same median rate of weight gain (Median= 1.5g/kg/day).

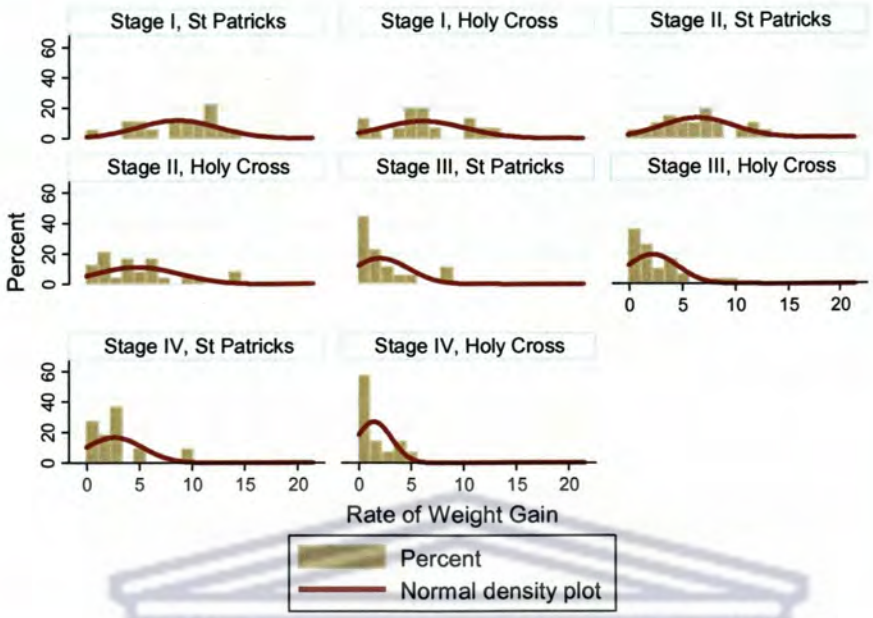

Figure 26.a: *Distribution of rate of weight gain by HIV status disaggregated by hospital*

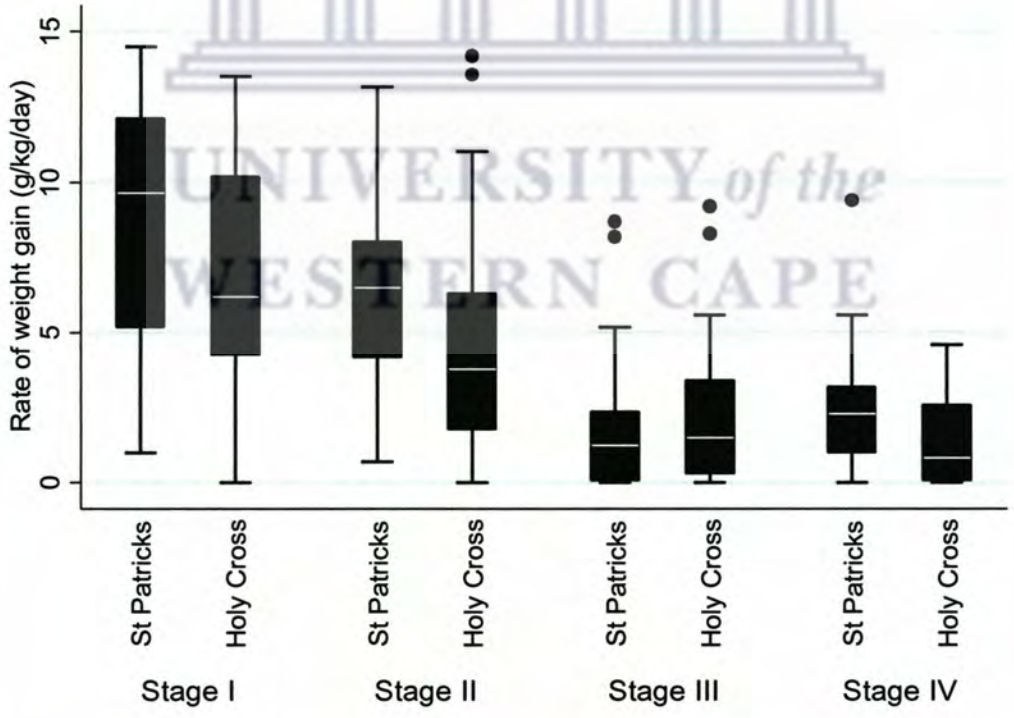

Figure 26.b: *Distribution of rate of weight gain by HIV/AIDS disease stage: Hospital-level analyses of discharged cases (2009 -2013)*

The same pattern of rate of weight gain across HIV disease stages observed using aggregated data was also observed when comparisons were made at hospital level (Figure 26.b). The median rate of weight gain decreased as HIV disease stage became more advanced.

Multiple comparisons between HIV disease stage and hospital settings using non parametric post-hoc methods showed that the differences between and within the two hospitals were statistically significant. The *p* values ranged between <o.ooo1 and <o.o1, except for the comparison between Stage 3 and 4 (p>0.05).

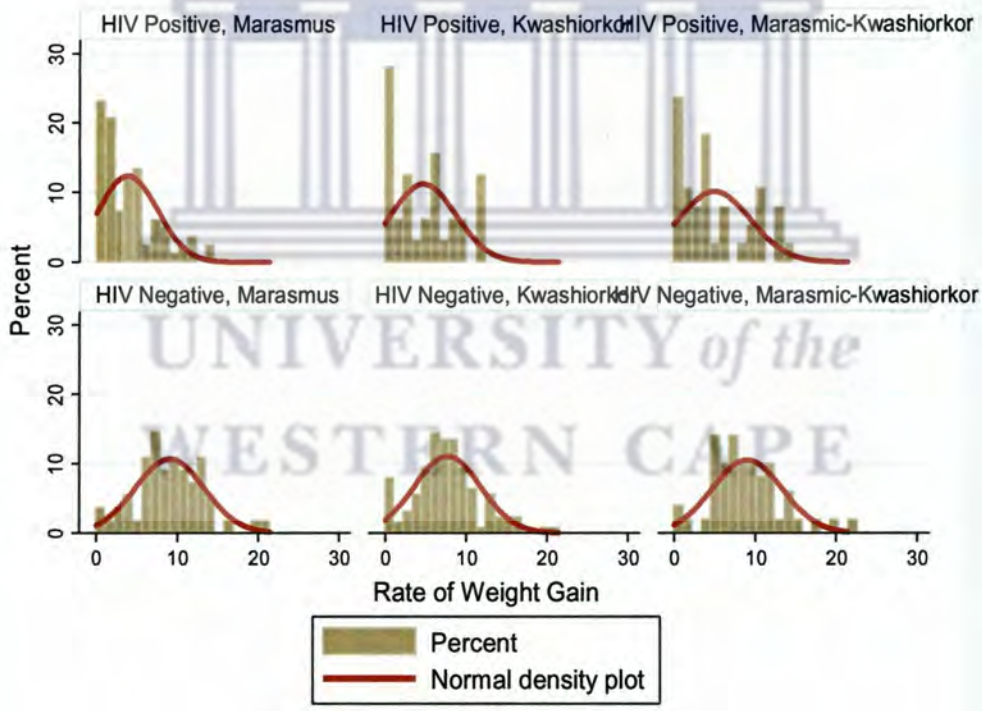

Figure 27.a: *Distribution of rate of weight gain by HIV status and SAM syndromic category*

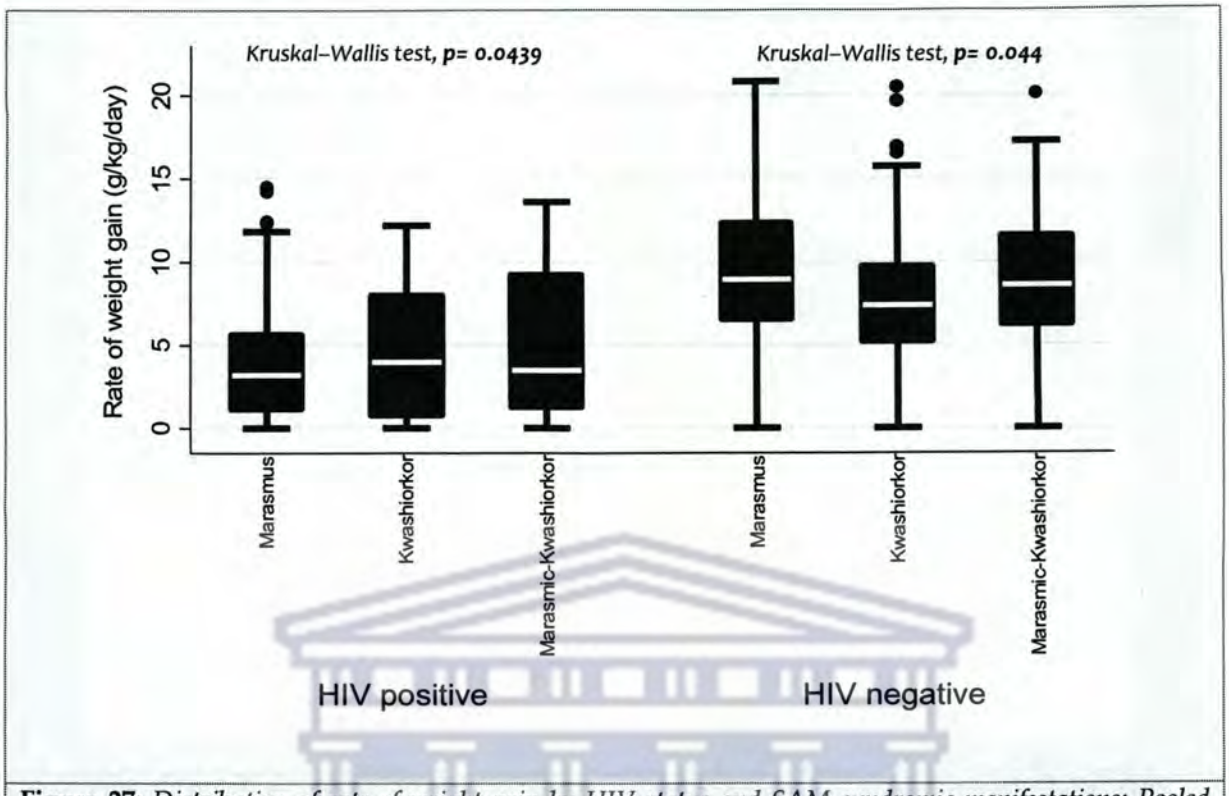

Figure 27: *Distribution of rate of weight gain by HIV status and SAM syndromic manifestations: Pooled analysis of discharged cases (2009 -2013)*

Figure 27.b compares the distribution of rate of weight gain among HIV infected and uninfected cases, based on the SAM syndromic variant they presented with at admission. The analysis is based on combined data from both hospitals. For HIV negative SAM cases with either marasmus or kwashiorkor or marasmic-kwashiorkor differed in terms of the rate of weight gain they achieved whilst in hospital. Marasmic cases gained weight faster, followed by those with Marasmic Kwashiorkor and lastly cases with kwashiorkor. However these differences were marginally statistically significant (p value ranged between 0.004 and 0.045). For HIV positive cases however, children who had Kwashiorkor showed a must faster rate of weight gain compared to the rest. These differences were however not statistically significant

However, the between-group (i.e. HIV positive vs HIV negative cases) differences in the rate of weight gain were notable. HIV negative cases who were marasmic had a higher median rate of weight gain (Median=9 g/kg/day) than HIV positive marasmic cases (Median=3.5 g/kg/day). Similarly, HIV negative SAM cases that had either kwashiorkor or marasmic kwashiorkor had higher median rates of weight gain compared to their HIV positive counterparts.

6.3. Duration of hospitalisation and clinical manifestations

The duration of hospitalisation reported here is only for cases that survived and were discharged following treatment. Although the criteria for patient discharge were not always fully followed, children were discharged if they completed a) the transition to catch up and were eating well, b) they had no oedema, c) had completed antibiotic treatment, d) had received electrolytes and micronutrients for at least two weeks, e) their immunisation was up-to-date and f) their road to health card had been updated.

Cases that died on the first day of admission were not included in the analysis as their inclusion in the analysis would have biased the comparative estimates based on clinical manifestations.

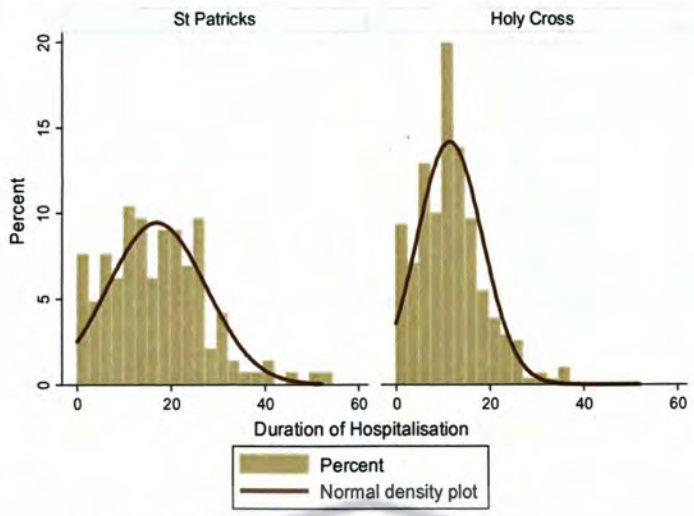

Figure 28.a: *Distribution of duration of hospitalisation by Hospital*

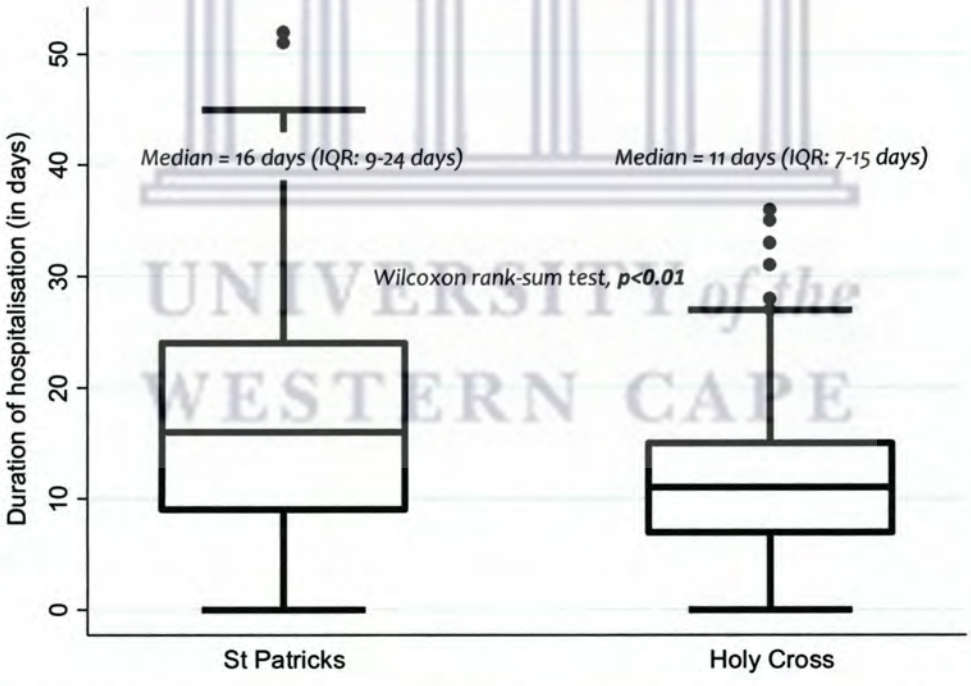

Figure 28: *Between-hospital Hospital comparison of duration of stay in the hospital Hospital for discharged cases, regardless of their HIV status (2009 - 2013)*

The Mann – Whitney U test revealed a statistically significant difference in the duration of hospitalisation between St Patrick's Hospital (n=144) and Holy Cross hospital (n=310) (U= 10324; Z= 5.454; p= <0.01). As shown in Figure 28.b, the median

duration of stay was higher at St Patrick's than Holy Cross Hospital (16 and 11, respectively), and the interquartile range was larger in the former compared to the latter.

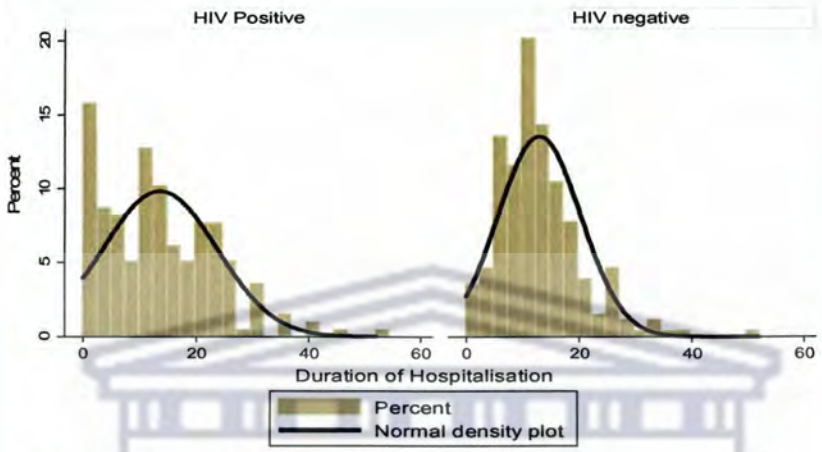

Figure 29.a: *Distribution of duration of hospitalisation by HIV status*

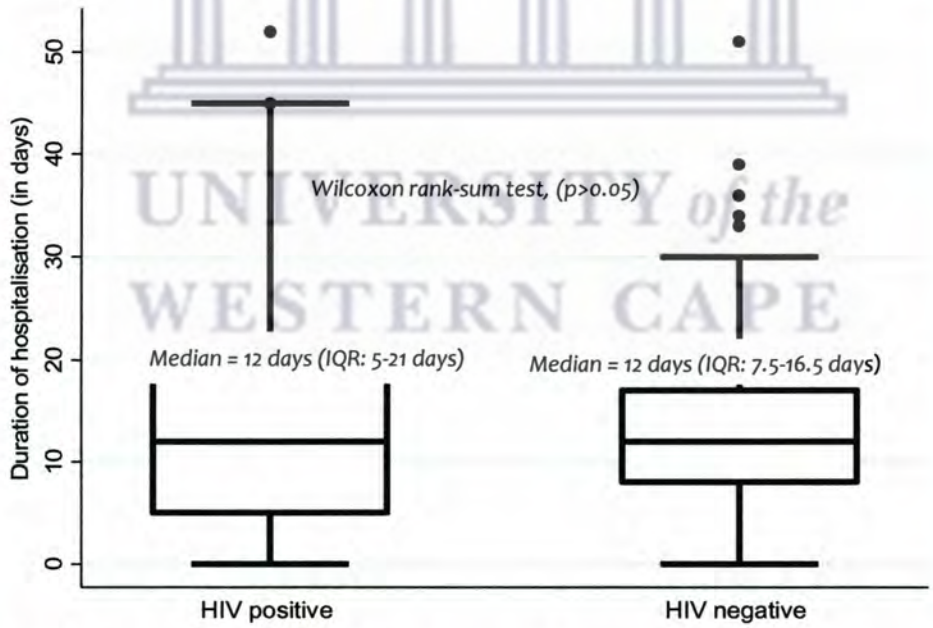

Figure 29.b: *Distribution of duration of stay in the hospital by HIV status: Pooled analysis of discharged cases (2009 -2013)*

The analysis shown in Figure 29.b is on aggregated data from both hospitals and compares days spent in hospital for HIV positive and HIV negative SAM cases. Wilcoxon rank-sum test showed that there was no difference in duration of stay

(p>0.05). However, there were some outliers particularly in the HIV negative group who stayed in the hospital for quite long (between 30 and 50 days).

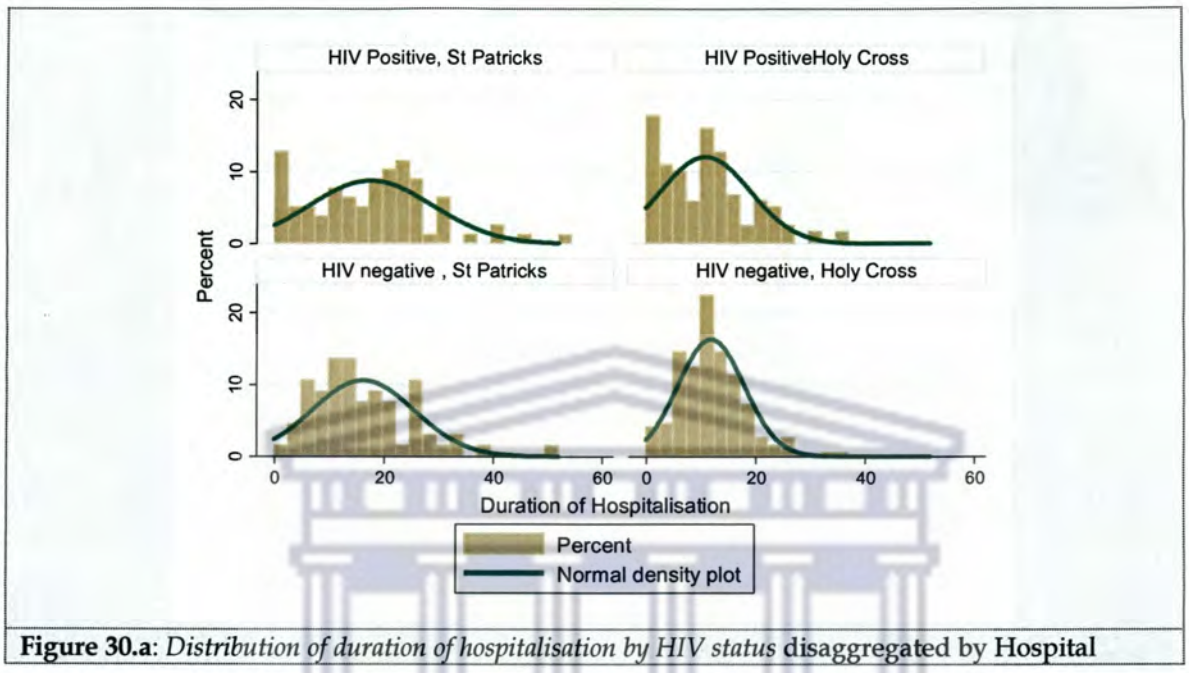

Figure 30.a: *Distribution of duration of hospitalisation by HIV status* disaggregated by Hospital

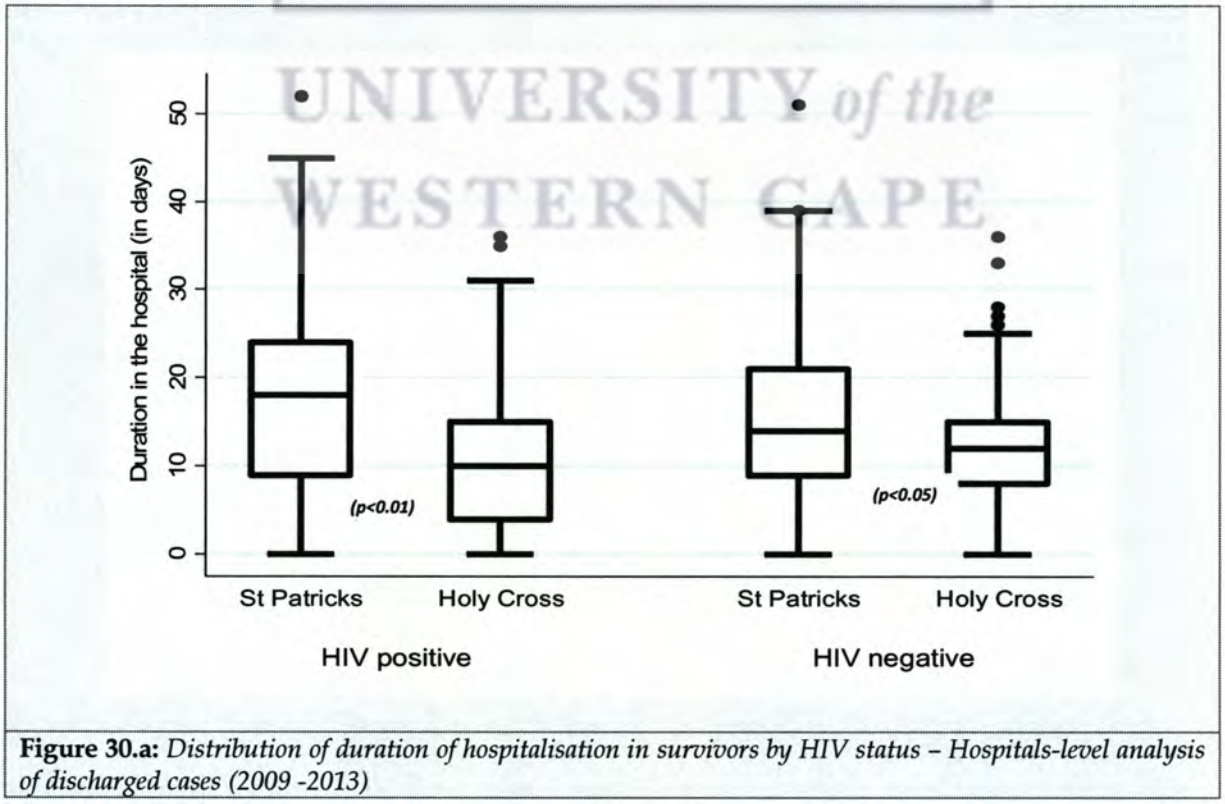

Figure 30.a: *Distribution of duration of hospitalisation in survivors by HIV status – Hospitals-level analysis of discharged cases (2009 -2013)*

When data were disaggregated by hospital, the same pattern was observed (Figure 30.a). The *within* - hospital comparison showed that the median duration of hospitalisation for HIV negative and HIV positive SAM cases were similar.

However, the median duration of hospitalisation *between* the two hospitals was different, with St Patrick's hospital generally recording larger medians for both HIV statuses than Holy Cross hospital. The median duration of hospitalisation among HIV positive SAM cases was 17 days at St Patrick's hospital and 10 at Holy Cross hospital, whereas for HIV negative SAM cases, it was 14 at St Patrick's hospital 12 at Holy Cross hospital.

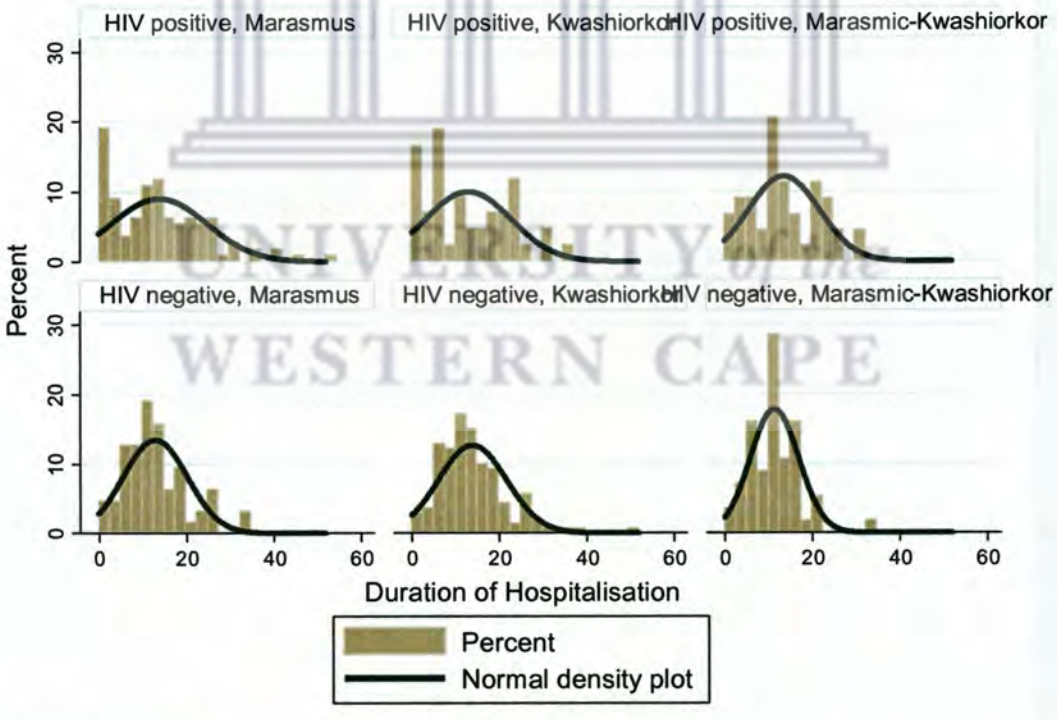

Figure 31.a: *Distribution of duration of hospitalisation in survivors by HIV status* disaggregated by SAM syndromic category

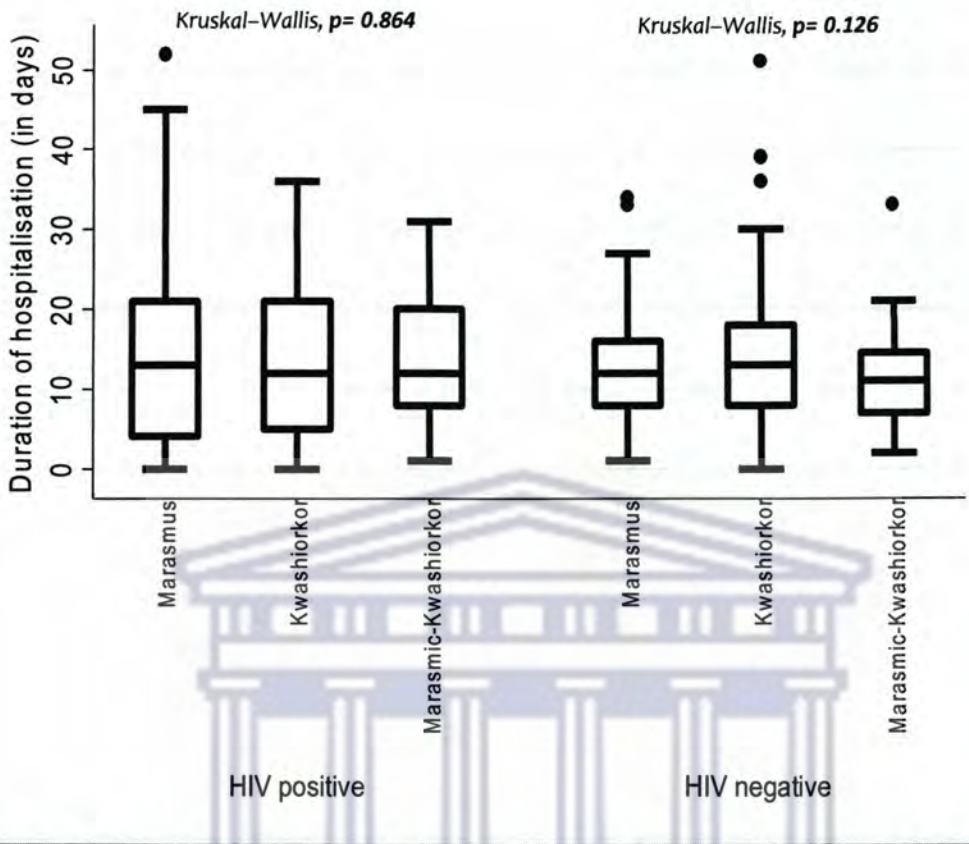

Figure 31.b: *Distribution of duration of hospitalisation in survivors by HIV status: Pooled analysis of discharged cases (2009 -2013)*

The results in Table 31.b show a comparative analysis of the distribution of days spent in the hospital among HIV infected and uninfected cases, based on the SAM syndromes they were diagnosed with at admission. Both the *within-* and *between-*group differences were not statistically significant ($p>0.05$). HIV negative children who had either marasmus or kwashiorkor or marasmic kwashiorkor had the same median duration of hospitalisation as their HIV positive counterparts.

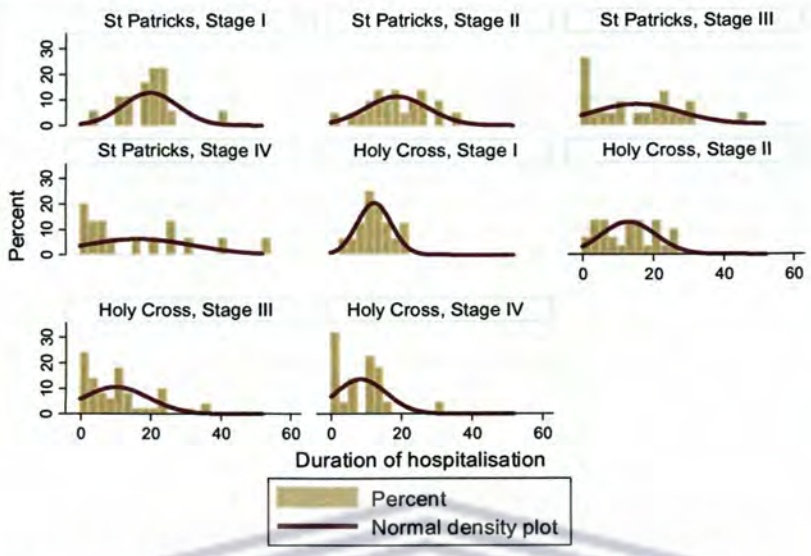

Figure 32.a: *Distribution of duration of hospitalisation in survivors by HIV status* disaggregated by HIV disease stage

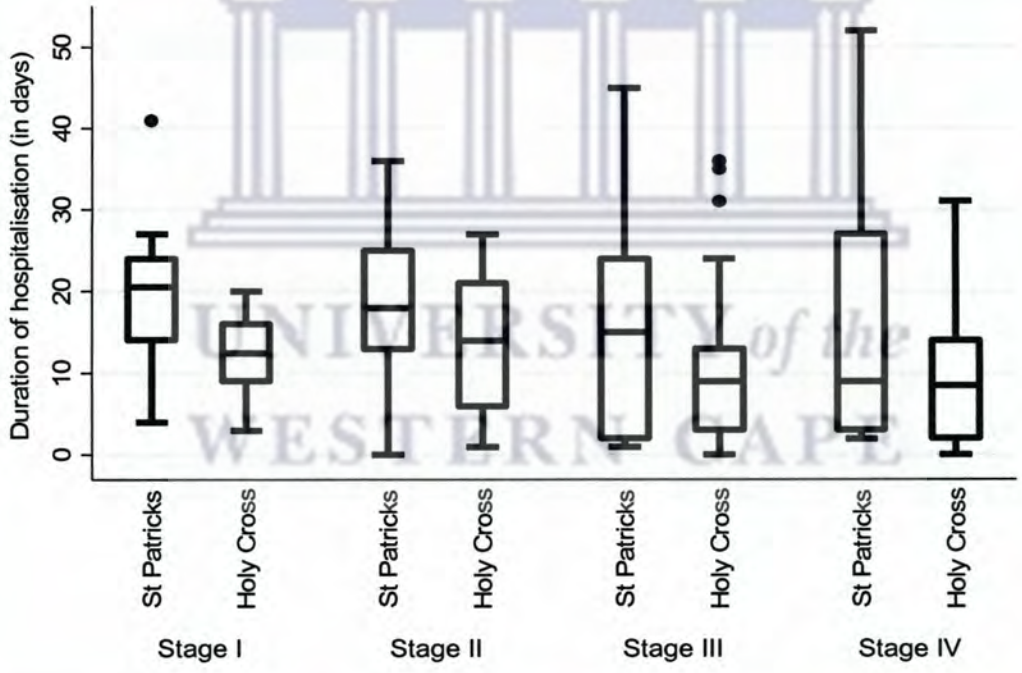

Figure 32.b: *Distribution of duration of hospitalisation by HIV/AIDS disease stage – Hospital level analysis of discharged cases (2009 -2013)*

When duration of hospitalisation was compared across HIV disease stages using hospital level data, the median duration of stay in the hospital tended to decrease as cases had advanced HIV infection. Multiple comparisons between HIV disease

stages in both hospitals using non parametric post-hoc methods showed that these groups differed significantly *within* and *between* the two hospitals. The *p* values ranged between <o.oooi and <o.oi, except in the case where Stage 3 and 4 were compared (p>0.05). The shorter duration for cases that were at Stages 3 and 4 may be due to the fact that most of them died two days following admission. However, for those who possibly survived, they stayed in the hospital the longest as shown by the long whiskers in Figure 32.b.

6.4. Relationship between rate of weight gain and duration of hospitalisation

The following results were also obtained based on the analysis of the data from children with SAM who were discharged following treatment. Estimates of the rates of weight gain used in this analysis were obtained based on the data from the period following the stabilisation phase.

Figure 33 shows mean rates of weight gain weighted on a number of SAM cases who were discharged during different time intervals.

The mean rates of weight gain at different time intervals were not significantly different between the two hospitals. In both hospitals, children with SAM who stayed between 6 and 12 days in the hospital showed a much faster mean rate of weight gain (>5g/kg/day) and those who stayed for a period less than 6 days achieved relatively poorer mean rate. However, the mean rate did not seem to increase beyond the 12 - 13 day interval of hospital stay, and the confidence intervals beyond this point began to widen. Wider confidence intervals were partly

due to few SAM cases at the end of the spectrum (Few SAM cases stayed longer than 20 days in the hospital) that were included in the localised weighting of the mean rate of weight gain. Wider confidence intervals were also observed for SAM cases that stayed for less than 3 days in the hospital as there were few such cases in this study.

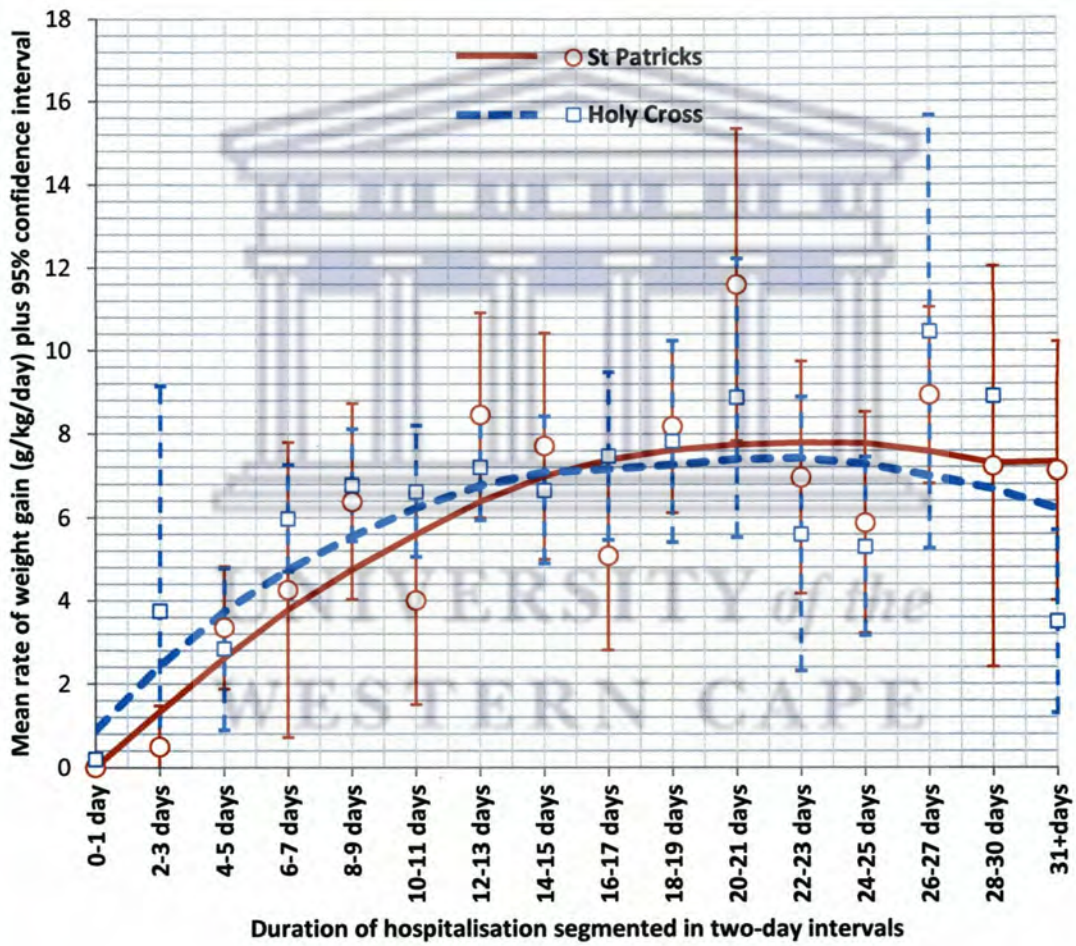

Figure 33: *Two-way scatter plot (fitted with polynomial smoothed lines and confidence intervals) for locally-weighted mean rates of weight gain and duration of hospitalisation (segmented in two-day intervals): Hospital-level analysis for cases that were discharged (2009 – 2013)*

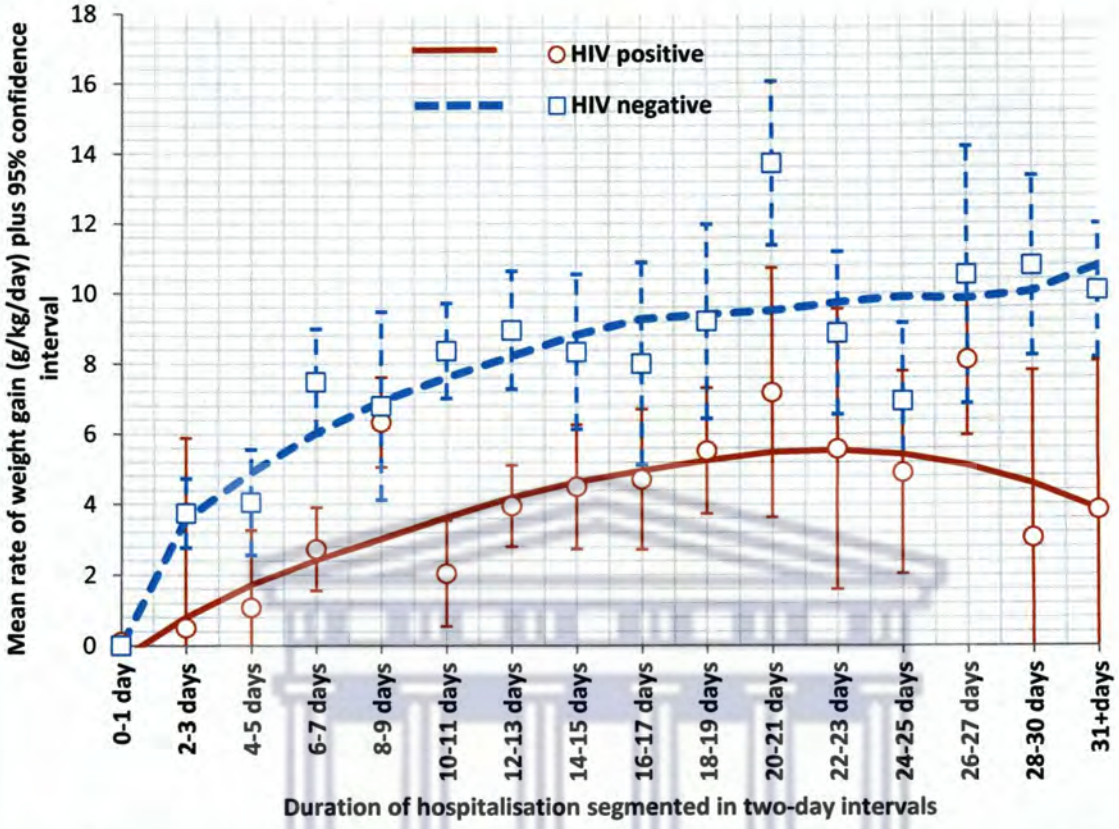

Figure 34: *Two-way scatter plot (fitted with polynomial smoothed lines and confidence intervals) for locally-weighted mean rates of weight gain and duration of hospitalisation (segmented in two-day intervals), stratified by HIV status: Pooled analysis (2009 – 2013)*

Since there were no significant differences between the two hospitals in terms of the mean rate of weight gain, it was reasonable to make comparisons of HIV positive and negative cases regardless of the hospital to which they were admitted.

As depicted in Figure 34, there were differences in the mean rate of weight gain between HIV positive and negative cases. The mean rates were consistently higher among HIV negative cases compared to HIV positive ones. In both cases, faster mean rates of weight gain were also achieved by children who were discharged between 6 and 14 days, after which point the rate plateaued. The mean rate for HIV positive cases that stayed longer in the hospital began to decrease from the 24th day

of hospitalisation. The fastest mean rate achieved by HIV negative SAM cases (5-9 g/kg/day) was when they were hospitalised until 5 to 14 days. For HIV positive cases, the mean rates were relatively poorer across all the time intervals.

This analysis, however, did not take into account SAM cases that had a negative rate of weight gain throughout the study period. There were 4 such cases from both facilities combined, but these were excluded from the dataset for the sake of analysis. The inclusion of these outlying values in the dataset significantly distorted the position of the polynomial smoothed lines which was fitted to the data.

6.5. Chapter summary

This chapter focused on the findings from the second part of Phase 2 of the study. The results showed that the rate of weight gain did not differ much between the two hospitals. However, duration of hospitalisation was much longer at St Patrick's hospital than at Holy Cross hospital.

With regard to HIV status, SAM cases that were HIV negative generally recorded a better rate of weight gain than their HIV positive counterparts. The analyses also revealed that there were no differences between HIV positive and HIV negative cases with regard to duration of hospitalisation among those who were discharged. However, when the data were disaggregated by hospital, some differences were found, with St Patrick's hospital recording longer duration than Holy Cross hospital for both HIV status categories. Furthermore, the study showed that the median rate of weight gain got smaller with advanced HIV disease stage, whereas the median

duration of hospitalisation became larger. These findings were observed during both aggregated and disaggregated data analyses.

The scatter plot showed that the locally-weighted mean rates of weight gain achieved at different time intervals were not significantly different between the two hospitals. Furthermore, HIV negative SAM cases attained a much faster mean rate of weight gain than their HIV negative counterparts within the same time interval. The rate of weight gain was much faster during the first few days following the stabilisation phase for both HIV positive and HIV negative cases, but levelled out almost after the 14th day following the stabilisation phase.

The next chapter will present the results from phase three of the study which focused on temporal analysis of mortality rates among SAM cases admitted during the study period.

7.1. Chapter introduction

The results presented in this chapter show how segmented regression analysis, using the Poisson approach, was applied to interrupted time series data. The aim of this analysis was to assess, in statistical terms, how much the discontinuation of the revised intervention changed three mortality outcomes related to SAM, immediately and over time. For reporting purposes, these mortality outcomes will hereinafter be referred to as *performance metrics* in each hospital. They are called performance metrics as they reflect the extent to which the two hospitals have, over time, performed to reduce mortality levels and trends associated with SAM, during and after the intervention.

The fully segmented Poisson regression models are presented. The corresponding line graphs which show the trend and level changes are also shown. The parameter estimates are reported in the tables as Incidence Rate Ratios (IRRs) which are exponentiated model coefficients for trend and level. The two-way line plots, on the other hand, consist of two interrelated lines. One line represents the observed monthly mortality rate for a specific metric measured over 69 months. The other line, which will be used to a larger extent to interpret the results, is a smoothed line which represents monthly model-predicted mortality rates for the same period. The analyses tested the null hypothesis that there would be no statistically significant increase in level and trend in the three indicators of mortality following the discontinuation of the revised intervention. Therefore, any statistically significant increase in these parameters for a given performance metric during the period after the removal of the revised intervention indicated a sustainability failure for that metric. Results for each performance metric in each hospital are presented side by side so that comparisons can be made.

CHAPTER 7

STUDY FINDINGS - PHASE THREE

Application of the Segmented Regression Model to Interrupted Time Series data to estimate the impact of discontinuing an intervention on mortality indicators related to SAM

Table 20: *Longitudinal analysis of total monthly SAM deaths relative to total monthly admissions due to SAM: Fully Segmented Poisson Regression Model, Incidence Rate Ratios (IRRs), Standard Errors (SEs) and p-values for each hospital*

Full segmented regression model	Holy Cross Hospital					St Patrick's Hospital				
	IRR	SE	95% CI		P value	IRR	SE	95% CI		P value
			Lower	Upper				Lower	Upper	
A_0 - *Intercept*	0.302	0.057	0.207	0.438	<0.001	0.164	0.057	0.082	0.327	<0.001
A_1 - *Baseline trend*	0.982	0.011	0.960	1.000	0.13	0.986	0.021	0.945	1.028	0.52
A_2 - *Level change after programme discontinuation*	0.390	0.172	0.164	0.927	0.03	1.905	1.060	0.640	5.673	0.24
A_3 - *Trend change after programme discontinuation*	1.051	0.019	1.012	1.091	<0.001	0.996	0.026	0.855	1.059	0.81

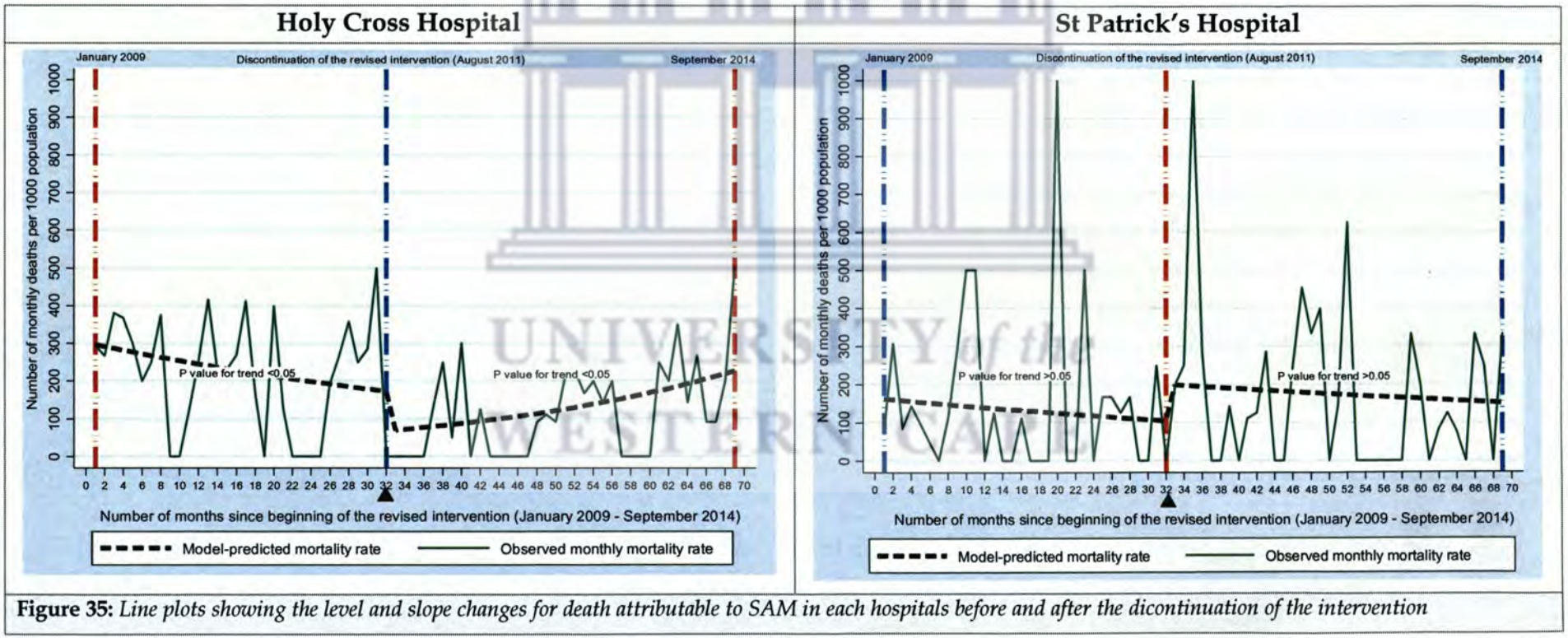

Figure 35: *Line plots showing the level and slope changes for death attributable to SAM in each hospitals before and after the dicontinuation of the intervention*

Based on the *model-predicted* line plots shown in Figure 35, Holy Cross hospital had higher *levels* of mortality rate per 1000 admissions during the intervention period compared to St Patricks Hospital. However, the *trend* (slope) in mortality was similar in both hospitals during the same period. Before the discontinuation of the intervention, the mortality rates attributable to SAM decreased by 2% every month in both hospitals. However, both these baseline trends were not statistically significant ($p>0.05$).

After the discontinuation of the revised intervention, the level of mortality due to SAM dropped by 61% at Holy Cross hospital within the first four months ($p<0.05$) whereas at St Patrick's hospital it rose by 90% within the same time period(>0.05). However, these sharp changes in levels of mortality only mark the beginning of the second segment of the interrupted time series (period after programme discontinuation). They do not reflect the immediate effect of discontinuing the intervention and will hereinafter be interpreted as such.

On the other hand, the trend changes following this data point reflect the potential effect of discontinuing the intervention. As shown in Table 20 and the model-predicted line plots in Figure 35, the trend in mortality rate after the discontinuation of the intervention rose significantly by 5% each month at Holy Cross hospital ($p<0.001$). At St Patrick's hospital, there was a month to month decrease of 0.4% after the discontinuation of the intervention which was not statistically significant ($p>0.05$).

Table 21: *Longitudinal analysis of total monthly SAM deaths within 24 hours of admission, relative to total monthly SAM admissions: Full Segmented Poisson Regression Model, Incidence Rate Ratios (IRRs), Standard Errors (SEs) and p-values for each hospital*

Full segmented regression model	Holy Cross Hospital					St Patrick's Hospital				
	IRR	SE	95% CI		P value	IRR	SE	95% CI		P value
			Lower	Upper				Lower	Upper	
A_0 - *Intercept*	0.098	0.032	0.051	1.188	<0.001	0.112	0.051	0.045	0.276	<0.001
A_1 - *Baseline trend*	0.985	0.019	0.947	1.024	0.45	0.961	0.031	0.901	1.024	0.22
A_2 - *Level change after programme discontinuation*	0.714	0.482	0.190	2.681	0.61	2.708	2.443	0.462	15.86	0.26
A_3 - *Trend change after programme discontinuation*	1.019	0.031	0.959	1.084	0.52	0.952	0.042	0.843	1.109	0.58

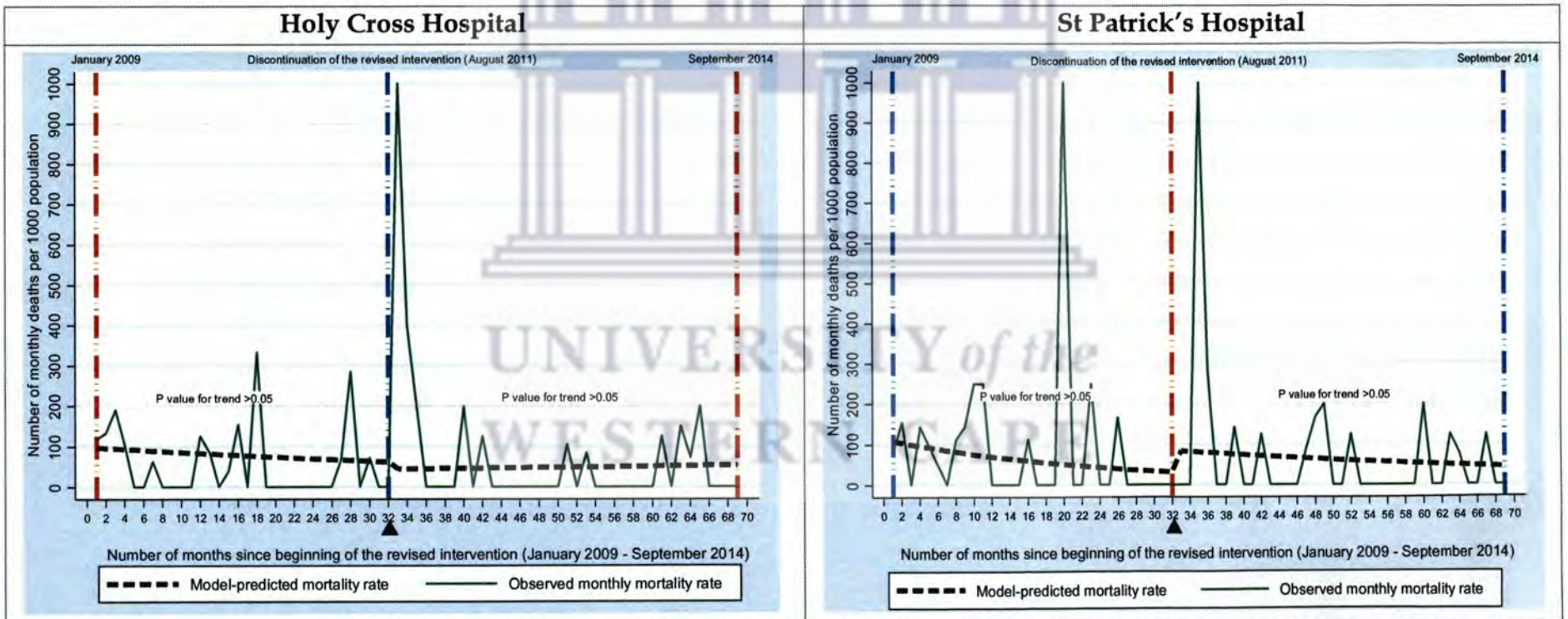

Figure 36: *Line plots showing the level and slope changes in SAM deaths recorded within 24 hours of admission in the two hospitals before and after the dicontinuation of the intervention*

Table 21 and Figure 36 show the results of fitting a Segmented Poisson Regression Model to the data on SAM deaths which were recorded within 24 hours of admission.

Based on the smoothed line plots and the reported IRRs, the performance of both hospitals in terms of reducing SAM deaths that occurred within 24 hours before the revised intervention was discontinued is comparable to a certain degree. Holy Cross hospital had a 1.5% monthly decrease in mortality rate within 24 hours which was not statistically significant ($p>0.05$). The 4% decrease in monthly death rate at St Patrick's Hospital during the same period was also not statistically significant ($p>0.05$).

However, the performance of the two hospitals on the same metric during the period after the intervention was discontinued was slightly dissimilar. At St Patrick's hospital, the trend in mortality within 24 hours continued to decline by 4.9% every month, whereas at Holy Cross hospital mortality rose slightly by 1.9% every month. These trend changes were nevertheless statistically insignificant ($p>0.05$).

In both hospitals, the levels of SAM mortality rate within 24 hours as predicted in the smoothed line plots, were higher at baseline (January 2009) than at the end of the study (September 2014). A much bigger difference between the two data points was observed at St Patrick's hospital. Similarly, in both hospitals, the model-predicted time series segment before the intervention was discontinued was higher than the segment in the post-intervention period.

Table 22: *Longitudinal analysis of the total monthly deaths due to SM & HIV infection relative to total monthly admissions: Full Segmented Poisson Regression Model, Incidence Rate Ratios (IRRs), Standard Errors (SEs) and p-values for each hospital*

Full segmented regression model	Holy Cross Hospital					St Patrick's Hospital				
	IRR	SE	95% CI		P value	IRR	SE	95% CI		P value
			Lower	Upper				Lower	Upper	
A_0 - *Intercept*	0.130	0.040	0.071	0.239	<0.001	0.080	0.040	0.030	0.213	<0.001
A_1 - *Baseline trend*	0.965	0.019	0.927	1.004	0.08	0.988	0.030	0.930	1.049	0.69
A_2 - *Level change after programme discontinuation*	1.839	1.205	0.509	6.648	0.35	1.730	1.397	0.355	8.428	0.49
A_3 - *Trend change after programme discontinuation*	0.961	0.032	0.909	1.076	0.72	0.993	0.039	0.919	1.072	0.85

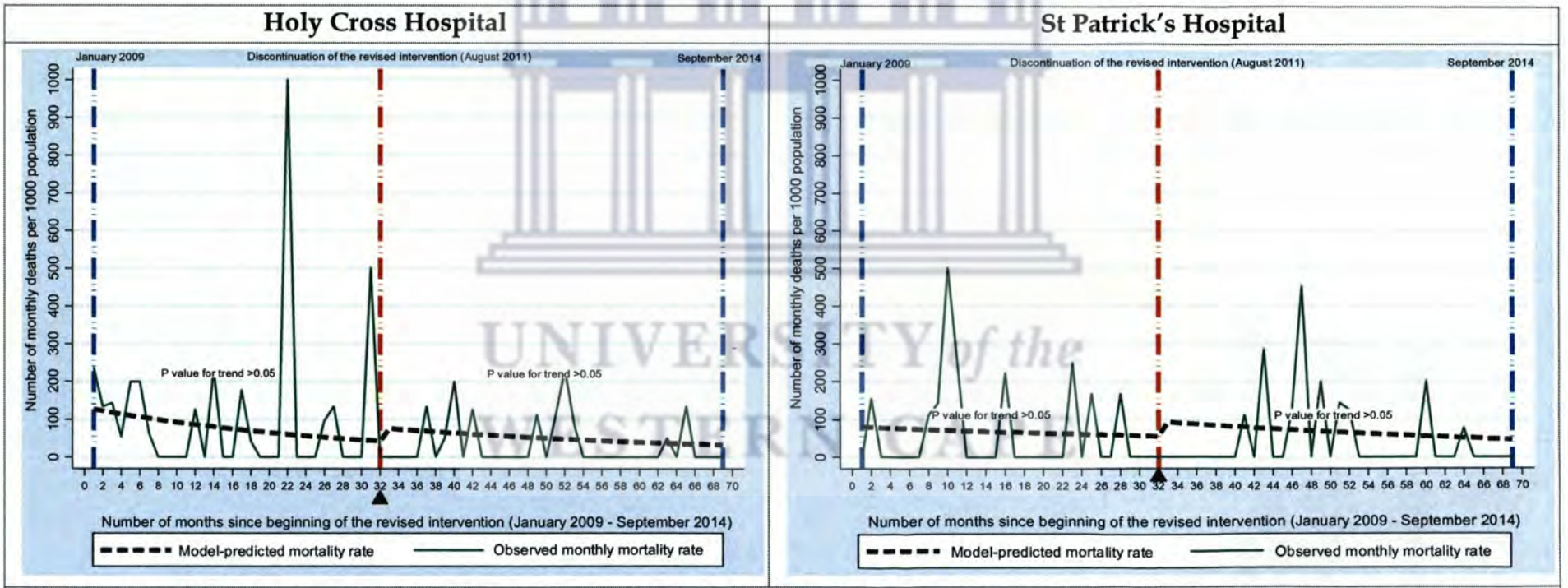

Figure 37: *Line plots showing the level and slope changes in deaths attributable to SAM and HIV/AIDS in the two hospitals before and after the dicontinuation of the intervention*

Table 22 and Figure 37 indicate that before the discontinuation of the revised intervention, there was a month to month decrease of about 4% ($p>0.05$) and 2% ($p<0.05$) in mortality attributable to SAM and HIV/AIDS at Holy Cross and St Patrick's hospitals, respectively. After the discontinuation of the intervention, the month to month mortality rates continued to drop in both hospitals even though these changes were not statistically significant ($p>0.05$).

These findings are an indication that the impact of the revised intervention may have been sustained even after it had been discontinued. Furthermore, the smoothed model-predicted line plots revealed that the endpoint mortality levels were lower than the baseline levels in both hospitals. This change was statistically significant and also indicates a likely improvement in hospital performance over time beyond the intervention period until the end of the study.

7.2. Chapter summary

This chapter presented results which attempted to show whether or not the study intervention was sustainable in reducing monthly mortality rates related to SAM over time.

Based on the null hypothesis set out at the beginning of the study, it was shown that the intervention was sustainable in improving three mortality indicators of SAM after it was discontinued. However, the total SAM mortality worsened every month after the discontinuation of the intervention at Holy Cross hospital, indicating that the programme was not sustainable for this metric.

It is the researcher's view that even though the observed changes in trends for some performance metrics were not statistically significant after intervention discontinuation, the conclusion about the sustainability of the programme in the post-intervention removal period should be considered with caution.

CHAPTER 8

STUDY FINDINGS - PHASE FOUR

Contextualisation and explanation of the quantitative findings

8.1. Chapter introduction

This chapter presents results from Phase 4, which aimed to:

- Explore the influence of key assumptions posited the intervention theory of change on implementation fidelity of the intervention, as well as
- Explain key findings from the quantitative phases 1, 2 & 3.

The themes that will be presented in this chapter include the explanations for critical illness and early deaths while hospitalised; the relationship between the rate of weight gain, duration of hospitalisation and patient discharge; Perceived effectiveness of the WHO guidelines; Perceived challenges related to the implementation of the guidelines; link between inadequate staffing levels after normal working hours and higher CFRs

8.2. Explanations for critical illness and early deaths while Hospitalised

The results from Phase 2 revealed that being critically ill upon admission was a major risk factor for early death in hospital.

Many hospital staff believed that there was a concordance of processes at household and community levels which often culminate in a child being critically ill and admitted late at the hospital. Subthemes that characterised the relationship between critical illness and early case fatalities during hospitalisation included: critical illness, traditional medicine practice and household child negligence; lack of disclosure, poor adherence to antiretroviral therapy and virological failure; misdiagnosis at the first point of care; and capacity to deal with complex presentations

8.2.1. Traditional medicine and household child negligence

Many participants reported that some parents and guardians of the children have consulted with traditional healers before bringing their children to the clinic or hospital.

> *"My office is based in the paediatric ward. I have observed a lot of cases there that are SAM related. ..... eehhh parents tend to first attend traditional medicines, you know, and they become too severe for these children to handle [interruption: Yes! - all agreeing], (**FGD - Social worker, Holy Cross hospital**)"....*
>
> *"The other thing we see commonly is the children who have deteriorated over a period of three weeks and they will have taken the child to the Sangoma (Traditional healer) first [interjected by exclamation] .....(**FGD – Medical Officer in charge of paediatric ward, St Patrick's hospital**)" ....*
>
> *From the laymen's point of view what also happens is that although they may know that the child is HIV positive but they still have those beliefs that may be the child was bewitched or something so they might not take treatment but may be take other routes, I think that also might contribute to high deaths (**FGD - Clinical support manager, St Patrick's hospital**)".*

The first visit to traditional healers often exacerbates the condition of the child such that by the time they get to the hospital they are critically ill due to herbal intoxication and other fatal side-effects associated with the use of traditional medicine.

> *So you can see the child has the signs of scarification or the signs of Sangoma visit and you ask when did you see the sangoma, they will say when the child got sick (**FGD – Medical Officer in charge of paediatric ward, St Patrick's hospital**)"*
> ....

Prolonged gross negligence of the child was also another factor cited by participants and considered to be contributing to critical illness and eventual death upon arrival at the hospital. Participants believed that some mothers choose to leave the child under the custody of their grandmother who may not be fit and able to look after the child. As a result, the child's condition may worsen over time in the absence of the mother and appropriate intervention.

> *"..... sometimes even the parents are not there, the children are staying with the grandmother, the parent is not there to take care of the child and the child will get worse because the grandmother does not have the resource and power to look after the child..... so such things play a very big role in what we deal with here at the hospital* ***(FGD - Social worker, Holy Cross hospital)".***

> *"The other thing is that the mothers underestimate the danger of infection and think that the child will try to survive. If they can be educated well enough may be it would change their perceptions and get to know that this is dangerous* ***(FGD - Pharmacist, Holy Cross hospital)"***

8.2.2. Lack of HIV disclosure, poor adherence to antiretroviral therapy and virological failure

The quantitative results also revealed that some SAM cases were admitted to the hospital at advanced stages of HIV infection and that such cases had worse treatment outcomes. They argued that most children with SAM who are admitted with HIV infection and with advanced HIV disease, have either been neglected by their mothers due to issues of stigma, or the mothers do not feel comfortable enough to disclose the HIV status of the child to those who take care of the child. Also, sometimes when the HIV status of the child is diagnosed at hospital level, some mothers choose not to adhere to antiretroviral therapy (ART) for themselves and the

baby. Most of the time, HIV infected mothers deliberately missed appointments for themselves and the child. Below are some quotes from two doctors at both hospitals which represent the dynamics of stigma, negligence and risk of death:

> *"The problems with those children who come in late with SAM and with low CD4 counts, you know, very [emphasizing the word "very"] ill children at advanced stages of HIV infection, is that I find that their mothers are very irresponsible. You will find that the child was born RVD positive. They will tell you that that PCR was done at 6 weeks and when you ask them did you do a follow up to get the results, they will say that no and may be they never even followed up on nevirapine, so the mothers can be very irresponsible. .... It is especially the younger ones (interruption by nurses: yes that is a problem). They are very irresponsible" (FGD – Medical Officer, Holy Cross Hospital)"*

> *"..... Another recurring theme in our hospital is lack of disclosure at home, we talked about the fact that the grandmother is looking after the children. So the mother knows she is RVD [retroviral disease] positive and the child has been exposed and she works away from home and she doesn't disclose the status of the child to the family so we have a lot of virological failures because she will only give the child ARVs because she herself is with the child, which will be intermittent (**FGD – Medical Officer, St Patrick's hospital)"***

8.2.3. Misdiagnosis at the first point of care

A clinician from one of the hospitals identified some gaps in the quality of care at the first point of care. In her view, sometimes the clinics or the community health centres where children with SAM are first seen before they come to the referral hospitals, do not provide the proper diagnosis for the child. As a result, children get worse over time and by the time they are referred to the hospital they are critically ill and beyond resuscitation.

".....and another reason will be that, the reason for mismanagement, or contributing to death of children is that when they come in , you don't know... they have been missed from the clinics, the diagnosis. The diagnosis is found here and by that time the child is in bad condition as they will have been treated for the wrong condition ***(FGD – Dietician, Holy Cross hospital)"***

In a separate personal conversation with one manager, the issue of misdiagnosis was also highlighted.

".. I think we should also invite some nurses from the primary health care centres within our catchment area where children are first seen before they are referred to us. They have a huge role to play in ensuring that we have a good enough continuum of care so that we don't have to deal with cases that have been misdiagnosed or have missing treatment history ***(Personal conversation with hospital manager, Holy Cross hospital - May 26, 2014, at 10h25)".***

8.2.4. Capacity to deal with complex presentations and the high risk of death

It was reported that some children with SAM present with complex conditions that a generalist medical officer may not easily detect or diagnose. This indicated that there was a lack of specialist physicians in the hospital.

".....but from a clinical perspective, one of the limitations is that because we are a level one hospital, and largely doctors who work in the paediatric ward are not paediatrician, we fail to pick up more complex presentations. So if you find TB difficult to diagnose and disseminated fungal infection or certain signs of meningitis will also be missed, and so, the risk is that these RVD positive children are not being treated appropriately for complications by the paediatrician. That may contribute to that earlier fatality ***(FGD – Medical Officer, St Patrick's hospital)".***

It was also reported that comorbidities that are present in some SAM cases also contribute to early deaths on arrival. This finding confirms the finding from Phase 2

of the quantitative study that found potential gaps in managing cases with complications other than SAM.

> *"Another thing is that when patients, or should I say children, come to the hospital they have multiple diagnosis, they have got pneumonia and TB (Tuberculosis) as well because the systems is affected. So they can be difficult to manage even though we implement the guidelines as we should* ***(FGD - Nursing service manager, Holy Cross Hospital)***".

8.3. Rate of weight gain, duration of hospitalisation and patient discharge

The quantitative findings revealed that the relationship between the rate of weight gain and duration of hospitalisation was such that generally SAM cases who were discharged between the 6th and 12th days of hospitalisation on average achieved a rate of weight gain of 5 - 7.5 g/kg/day. This was way below the target rate of weight gain of more than 10g/kg/day. The results also indicated that the median duration of hospitalisation for some SAM cases that survived was below 10 days, and that at Holy Cross hospital the duration of stay in the was on average shorter compared to St Patrick's Hospital. The most striking reasons for the observed differences in duration of hospitalisation was that the decision to discharge SAM cases did not depend entirely on whether they had achieved sufficient weight gain. Some other factors were involved in the decision-making process. For instance at Holy Cross Hospital, it was observed that when there are shortages of beds, a slight improvement in terms of weight gain often led to premature discharge of the patient.

"Sometimes there is no space in the ward so if the child has got appetite you discharge them but right now we have space ***(Field notes – opportunistic conversation with a nurse, Holy Cross hospital, June 2011, 10h00)"***

".....I wasn't aware of the national guidelines regarding discharge but our biggest limitation is bed availability..... [Nurses interject with a YES]. So what limits us is that during the dry season is when we have a lot SAM cases, and as soon as you have a number of the critical ones that's when you move around the ward and say you look better you should go home and that is regardless of whether they have gained weight and are stable. But we do follow them up; the dietician will see them every two or six weeks after discharge ***(FGD – Medical Officer, St Patrick's hospital)".***

Another interesting finding was that the discharge criteria for SAM cases as indicated in the WHO guidelines were not consistently followed; in favour of national guidelines for discharging a patient. As shown in the quote below from the nursing service manager at St Patrick's hospital, there is a requirement by the hospital to discharge patients within five days of admission.

"Oh okay, thank you. Ummhhh ... the thing is that we have national guidelines by which we have to comply because we don't have to keep the patients, it should not be more than five days. It is a national norm ***(FGD - Nursing service manager, St Patrick's hospital)".***

Another reason for discharging SAM cases was that sometimes there is no food to give the children and therefore it was considered pointless to keep them hospitalised.

"Yes it would be a good idea to allow children to stay longer in the hospital if the resources are there, but because of (processes) of food, no milk, nothing and the mothers would love to go home,.... Even us we are not happy because there is no food

to give them. It doesn't make any difference if there is no food here and there is no food at home. So it is better for them to go ***(FGD- Nursing service manager, Holy Cross hospital)".***

"There were some children who were admitted for two weeks and they were getting better but the problem is that we did not have protein to give them so I felt that instead of keeping them and waiting for something we don't know I said let me just discharge this child and have the dietician counsel the mother on what she must give the child ***(FGD – Medical Officer, Holy Cross hospital)".***

The doctor from the same hospital also argued that discharging them earlier, particularly when there is no food to give them, prevents them from contracting other infections they are exposed to in the hospital. He also argued that in some instances, mothers realise there is nothing to give the child and request that they get counselling on how to feed their child so that they can be discharged early.

"Like sister said. It is pointless to keep them here while we are doing what was being done initially. You are not helping them by keeping them here without food mothers realised *exposing them to more infection because it is not only SAM cases that you get here and they have low immunity so there is a chance of getting other infections. So it is a practical solution but it has its cons* ***(FGD – Medical Officer, Holy Cross hospital)".***

" ..... Also sometimes the mothers have access to the child support grant but did not know what to feed the child. So if they realised that there is not food in the hospital, the dietician can counsel them on what food to give the child and they can be discharged sooner. That is why it is important that we tell them to come back here to see that what you told them to do is being done ***(FGD – Medical Officer, Holy Cross hospital)".***

A question was asked about whether participants believed there was a link between relapses (or readmission) due to SAM and premature discharge before children

attained a reasonable rate of weight gain. This question was particularly prompted by an observation made by the researcher during the course of the study where he conducted a short investigation into this problem and found that 70% of the cases who were readmitted to the hospital were those who were discharged before they recovered fully (***Field notes - Holy Cross Hospital, August 2010, 14h25***). Generally, participants from both hospitals believed that there was no relationship between premature discharge and relapses. Some participants reported that mixed feeding was the leading factor for readmission rate at their hospital.

> *"Ummhh!!!!! I don't think that is the problem really. The problem is generally mixed feeding [Interruption, Yah! All in agreement]. The babies are staying with their grandmothers who can't breastfeed the child and they choose to give them whatever food there is at home, so..... (**FGD – Maternity nurse, Holy Cross Hospital**)"*

Some of them also felt that following up discharged cases was still an issue and that they had challenges with community outreach programme to ensure that relapses are kept at a minimum. Below is a quote illustrating what participants had to say regarding the issue of follow up and outreach.

> *"I think the logic is that there should be more outreach and home visits and also visiting clinics. But the problem is actually we are short-staffed; we don't have enough capacity to do outreach. So it causes a lot of relapses (**FGD – ward nurse, Holy Cross Hospital**)".*

8.4. Perceived effectiveness of the WHO guidelines

Some participants felt that the guidelines were useful and easy to implement.

*"I think in terms of the guidelines, especially the nurses, this is something we do quite well. They are straight forward [yes, they are easy to follow! All in agreement].....(**FGD- St Patrick's Hospital, Medical Doctor**)"*

This response from the doctor was however contradictory to what emerged in a separate FGD with junior nurses at the same hospital. It was clear that even though the nurses had been in the ward for more than six months, they were not entirely comfortable with the use of the guidelines. This shows that the systems that were put in place during the study period to ensure that all the new rotating nurses got inducted in the ward in order to be able to use the guidelines were not entirely sustained thereafter. In a follow up question regarding the perceived usefulness of the guidelines, the nurses were asked whether they had been trained on how to use the guidelines and whether they were comfortable to use them. Three out of five nurses who were in the focus group were neither trained nor comfortable to use the guidelines.

Another interesting dimension to the effectiveness of the guidelines was that it was only helpful for cases that were not critically ill. A dietician from St Patrick's hospital who was responding to a probe about why there are still some poor outcomes in some months said that this was due to some cases that were going to die despite the full implementation of the guidelines.

*".....sometimes we do get those cases like you mentioned those that die within 24 hours, they come in critical and then they end up dying with your initial treatment. So with the guidelines, the guidelines are implemented very well so I think it is one of those cases that will die anyway (**FGD- St Patrick's hospital, Dietician**)".*

It was interesting to learn that there were no differences in opinion regarding the relative effectiveness of the guidelines for HIV positive and their HIV negative counterparts. Most FGD participants, particularly the nurses, seemed to be of the view that the guidelines should work well regardless of HIV status. Below is a quote from one nurse at Holy Cross hospital to which the rest of the nurses seem to react in the affirmative.

> *"I don't think the outcome would be different because of HIV infection: I think the outcome would be the same, if really we were at par with the training on SAM [Interjection – Yeah! Most nurses agree] (FGD - St Patrick's hospital, ward nurse)".*

8.5. Some challenges related to the implementation of the guidelines

The challenges related to the implementation of the WHO guidelines fell into three subthemes namely: The changes in the skilled personnel to sustain quality of clinical care; the sporadic shortage of therapeutic resources; and the organisational and system-wide challenges

8.5.1. Changes in the skilled personnel to sustain quality of clinical care

A dietician at Holy Cross hospital stressed the importance of constant training. She indicated that this was one of the reasons why they sometimes have differences in outcomes over time, alluding to the possibility that there are some months wherein SAM cases are managed by relatively inexperienced clinicians (doctors and nurses alike) who are not familiar with the guidelines.

> *"No the guideline are working very well… it is just that may be in some intervals or period, training needs to be done, because there is rotation of nurses , sometimes there*

is also changes of doctors responsible for the ward. So there needs to be constant training of nurses. ....I feel there is a gap there, but in terms of classification, I don't think that everyone is on par with the classification of malnutrition, and may be that is why we might not be managing some patients as well as we should ***(FGD- Holy Cross hospital, Dietician)***".

This particular finding corroborates what was observed by the researcher at the beginning of the study in both hospitals. The challenge for the researcher during all the short visits to the hospitals was to get the rotating nurses on board with the WHO guidelines by providing informal training especially at night when there were no experienced nurses on duty to look after the SAM cases. Below is one excerpt from the field notes which highlights the issue of training in achieving optimal implementation of the guidelines:

The turnover of the nursing staff is still a challenge particularly at Holy Cross Hospital. Although some improvements have been made in terms of maintaining a reasonable and constant number of nurses who are well trained in the implementation of the SAM treatment protocol, some fairly new training nurses still get deployed to the paediatric ward for mandatory rotation and inevitably end up handling SAM cases. At St Patrick's Hospital, however, there seems to be a stable team of paediatric nurses and the chief nurse has been proactive in ensuring that nurses are doing the right thing or even doing everything herself when junior nurses seem to fall short ***(Field notes - both hospitals at different times, February 2010)***.

8.5.2. Sporadic shortage of therapeutic resources

Another challenge that seems to have been persistent over the years was the sporadic shortage of resources particularly the required ingredients to prepare starter and catch-up formula for the SAM cases. This issue was identified both during observations and the FGDs. As will be shown later in this chapter, this

challenge is sometimes a result of inefficient support services that are independent of the facilities.

> *"Sometimes we do not have mineral mix and some types of drugs or even ingredients for formula feeds..... So we have to use our own money to buy for example milk or sugar (**Field notes - Observation and a personal conversation with one of the front line health care givers, St Patrick's Hospital, June 2011**)".*

> *"This other time we saw the sister in charge and she was so excited because she had CMV. She said that when we have CMV we discharge them healthy but when we run out of CMV then there is a problem. So we are actually experiencing problems because sometime we run out and it is not even a good idea to buy a large quantity because they expire quickly so for you to order again that is another process, it is gonna take time to get it here (FGD- St Patrick's Hospital, Dietician)".*

Some challenges related to the execution of specific procedures stipulated in the guidelines were also highlighted. In particular, treatment of shock was one aspect of the guidelines which came up as problematic during quality care assessment in Phase 2 of the study. When asked about some of the reasons why treatment of shock has not been adequately done, this is what one doctor had to say:

> *"With regards for example to the treatment of shock, the problem is that I am not able to see what I am treating. I just treat blindly, because we don't have a blood gas machine. In my training I was told that when you are giving a child the fluids you must know what you are dealing with. Most of them will have hypokalemia and hyponatraemia so you have to know what you are giving and how much of it you should give and you have to monitor how the child is responding..... Yes I do it, I give the fluids, but if we could get something that we could use to monitor the micronutrients with, it will be of great help (**FGD – Holy Cross Hospital, Medical Officer**)".*

8.5.3. Organisational and system-wide challenges

In both Hospitals, particularly at Holy Cross hospital, there seemed to be an inefficient and fragmented procurement system. During a personal conversation with the procurement officer at the beginning of the study, this issue was explained. According to her, there was a problem with a number of bureaucratic channels through which most requests for supplies have to go. For example orders are made from various hospital units then tabled to the management committee which needs to meet to make a decision. The endorsed requests/orders are then sent to the district office in Lusikisiki (A small town situated about 45 km away) which is highly understaffed and inefficient and as such accumulates all the orders for a number of days pending their review. When a go-ahead has been issued, only then can the orders be taken to Mthatha (a much larger town farther away from the facility) where they are dispatched to different facilities ***(Field notes - Personal conversation with the procurement officer at Holy Cross hospital, June 2011).***

Although this problem was observed at the beginning of the study, it seemed to have persisted throughout the study period. Below is what some participants from both hospitals had to say regarding the current procurement system at their facility:

> *"You see, we have a problem with people who are given tenders to supply some resources to the hospital. Sometime they take time and it can get frustrating because at that point it is out of our control* ***(Field notes – personal conversation with a pharmacist St Patrick's Hospital, 16 May 2014 at 11h00)****".*
>
> *"We have ahhh, I don't know ..... system problems. Delays when trying to approve the orders, service providers not complying or not being able to deliver what they are supposed to deliver even if the orders have been approved... [Interjection by one*

nurse, Yeah BEE - which stands for Black Economic Empowerment]. Supply chain, that is where everything sort of gets stuck ***(FGD – Holy Cross Hospital, Dietician)".***

Inefficient communication channels between the hospital and the laboratory facilities were also reported as one of the organisational challenges. The laboratory serves as a support structure to the facility by assisting with the evaluation of blood samples and conducting other clinical examinations on patients' specimens. This was a particular problem at Holy Cross hospital and it seems to have persisted over the years. Generally, orders for blood tests are sent to the laboratory but the results do not come back soon enough for the clinician to make some crucial medical decisions.

"The problem with the lab is that even though they operate in-house they tend to say that they have a problem with staff and they cannot process the results as efficiently as you would like. It is more doable with a blood gas machine. With the lab you have to take a lot of specimens and the bottles are big. And the delay is a problem because by the time you get the results you are ready to send in another specimen for lab evaluation. So most of the time you are just treating them blindly hoping that they will recover ***(FGD – Holy Cross hospital, Medical Officer)".***

Medical doctors at Holy Cross hospital also highlighted that the Department of Health was still reluctant to ensure adequate human resource capacity in the hospital, particularly specialist clinicians ***[Field notes - Personal conversation with the hospital manager, Holy Cross hospital, August 2012]***. At the beginning of 2011, there were only 6 medical doctors none of whom had a specialty in paediatric medicine. By May of the same year, two had left including one who had shown consistency and dedication in providing paediatric care. The pharmacist and the only one dentist had also since left and none of these vacancies had been filled yet at

the time ***[Field notes - Personal observation, September 2011]***. Furthermore, some doctors would go on long annual leave, thereby leaving the remaining doctors overworked and unable to attend to all wards as and when requested by nurses during emergency situations. As a result some cases are not attended to and may eventually die **[*Field notes - Personal observation, June 2011*]**.

However, this challenge seems to have been addressed gradually during the course of the study. As will be shown in the quotes below, there might be a link between the improvement in staffing levels 0f doctors and the performance of the hospitals over time. At St Patrick's Hospital, when a question was asked about what changed in the hospital which might have led to improvements in some outcomes in terms of mortality attributable to SAM over time, one doctor had this to say:

> *"I know I wasn't here until 2013 but I think one of the reasons I could associate with that pattern (improvement in mortality) is that there was bad staffing, especially of doctors. so if you got three doctors managing the whole hospital you gonna have a doctor that is gonna be tired most of the time so they are not gonna perform to their level best because there is many patients to see, so I think that was the major factor* ***(FGD – St Patrick's hospital, Medical Officer)***".

A nurse at St Patrick's hospital also had this to say in relation to this subject:

> *".....and also, going back to the issue of case severity and herbal intoxication as the leading factor for mortality, it is now different because we now have doctors that can see patients and monitor them and do follow up* ***(FGD – St Patrick's hospital, nursing service manager)***".

8.6. Inadequate staffing levels after normal working hours and higher CFRs

The quantitative phase of study revealed that generally more than 60% of the fatalities occurred after normal working hours. When participants were asked what might have accounted for this pattern some believed it was because there is poor staffing at that time, while others argued that it might be because frontline health care workers are too tired to attend to the children who are in a critical condition. The two quotes below illustrate this interpretation:

> *"Maybe the kids are not getting feeds at this time because the nurses are relaxing, I don't want to say they are sleeping but kids are not getting their treatment as they should (**FGD – St Patrick's hospital, Nursing service manager**)".*

> *"You know the condition changes at night, so you know during the day it is better because you can get the doctor to come… I wouldn't say that it is because the doctor is not called it is just that may be there is no that urgency to call to come and see that child whose condition is changing (**FGD – Holy Cross hospital, Dietician**)".*

Figure 38 summarises some factors identified during the ethnographic and FGD enquiries, as contributing to high case fatality rates for SAM in the study setting.

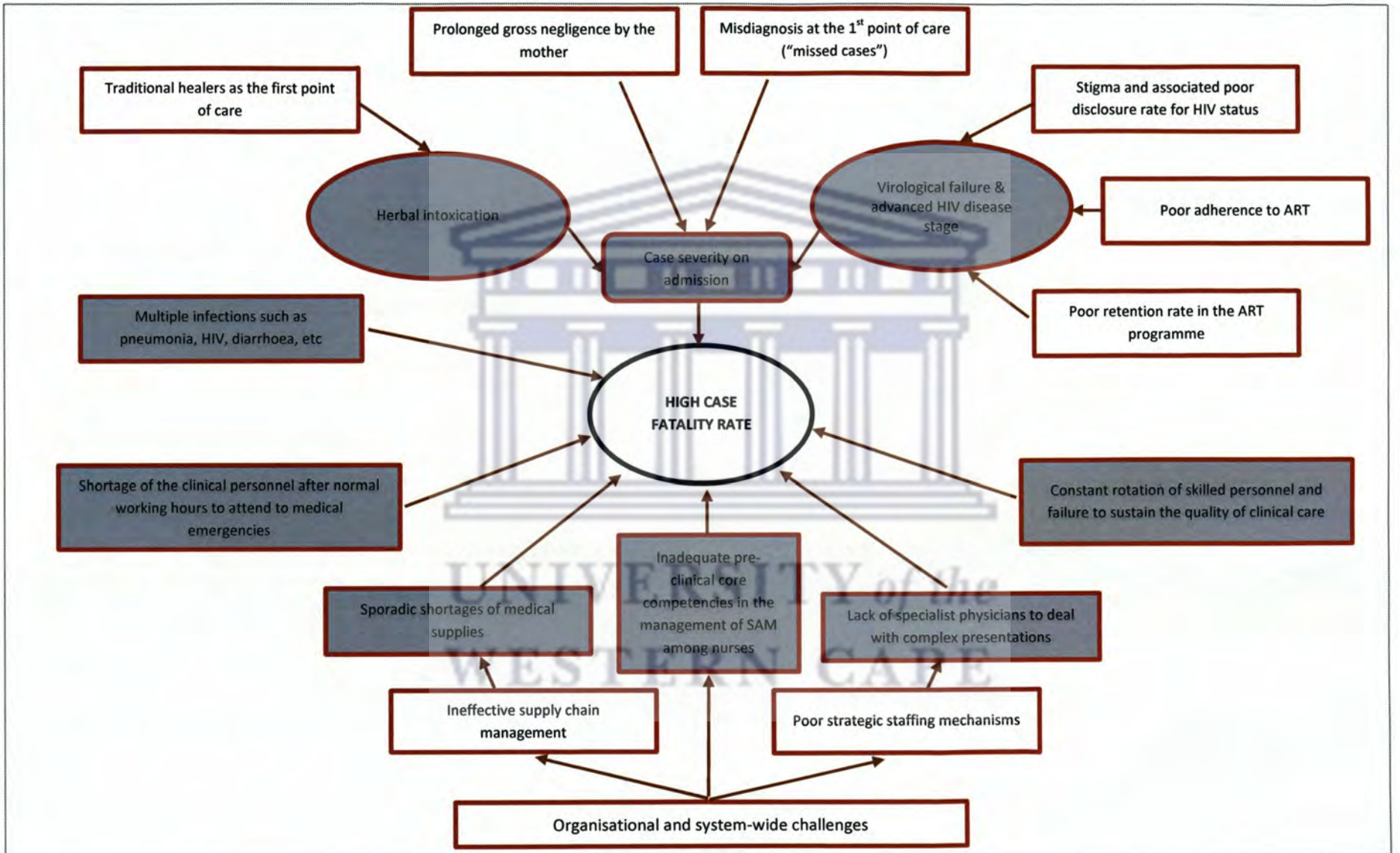

Figure 38: Some *factors believed to contribute to high case fatality rates for SAM in the study setting*

8.7. Summary

The results presented in Chapter 8 put the quantitative findings into context. The results show how some of the assumptions underlying the intervention theory of change can influence the effectiveness of the intervention developed as part of the study. The potential moderating factors not studied in the quantitative phase were also highlighted during this chapter.

The health care workers interviewed in each hospital believed there are some processes which precede critical illness. These included for example: traditional medicine beliefs and practices, gross negligence of the child at household level, lack of HIV disclosure which within the family may lead to poor ART adherence and eventually virological failure, and misdiagnosis at the first point of care. Participants who took part in this Phase of the study also confirmed the results presented earlier in Chapter 5; that being critically ill on admission was associated with the high risk of death. Another factor believed to be associated with the high risk of death was the lack of human resource capacity in the hospital to deal with complex presentations.

The results also highlighted that discharging SAM cases did not depend entirely on whether they had achieved sufficient weight gain. Some other factors, including shortage of patient beds in the ward, policies to discharge patients within five days of admission and sporadic food shortages were at play.

With regard to the implementation of the WHO guidelines, health care workers generally felt that the guidelines were effective and relatively simple to implement, but that they do not make much difference among SAM cases that are admitted in a

critical condition. They also believed that the effectiveness of the guidelines was not different in respect of HIV status, a finding which contradicts what was shown in the two quantitative phases. Some challenges believed to hinder adequate implementation of the guidelines include a) the lack of continuity in training of rotating nurses as well as newly appointed medical officers, b) sporadic shortages of therapeutic resources, c) inadequate staffing levels after normal working hours, and d) some organisational and system-wide challenges beyond the immediate control of clinicians.

CHAPTER 9

DISCUSSION

9.1. Chapter introduction

This operations research started with a review and improvement of a longstanding guideline-based intervention which was originally developed to improve the management of SAM in two rural district hospitals in South Africa. The resultant intervention was then implemented and evaluated.

The initial evaluation focused on the epidemiology of SAM among severely malnourished children before and after they were treated in the context of the revised intervention. Here, the effects of HIV infection, disease stage and other clinical characteristics on morbidity and mortality profiles of SAM cases were assessed. The relationship between the rate of weight gain and duration of hospitalisation based on HIV status and disease stage were also evaluated following treatment.

The second evaluation sought to contextualise the effectiveness of the revised intervention in improving treatment outcomes. This was achieved by exploring a number of moderating factors which were theoretically preconceived as potential influencers of implementation fidelity. Lastly, the study evaluated the sustainability of the revised intervention beyond the study period.

In this chapter, the results from the entire study are discussed. The discussion is at the level of the study phase. However, the findings from Phase 4 will not be discussed separately. Since Phase 4 consisted of an explanatory enquiry, the findings from this phase will be used to support the discussion around the three other phases. For each study phase, the discussion firstly pulls into focus the extent to which the

study hypotheses have been addressed. All the major findings which support or do not support the stated hypothesis are explained. The explanation aims to situate the meaning of the findings within the context of the existing literature, the theoretical frameworks used, and practice at large.

The discussion also touches on the limitations and strengths of each study phase as well as the study as a whole. Based on this, some possible future research questions and methodologies to be considered are also highlighted.

9.2. PHASE TWO - PART ONE: Risk factor epidemiological modelling of SAM in the context of the WHO "10-steps" treatment guidelines

The first part of Phase 2 focused on eight hypotheses. The first hypothesis stated that there would be no statistically significant differences between the two hospitals in terms of the clinical characteristics of SAM cases on admission. This hypothesis sought, in part, to answer the question about whether there were similarities in the morbidity profile of children who come from two geographically distant areas. The findings from this study support the stated hypothesis to a large extent. Apart from the distribution of SAM cases by HIV status which was different between the two hospitals, other clinical characteristics were similar. At St Patrick's hospital, there were more HIV infected cases than their uninfected counterparts.

One explanation of the differences in the distribution of SAM cases by HIV status between the two hospitals is the selection bias The SAM cases admitted at each hospital were purposively selected from patient records using pre-determined

inclusion and exclusion criteria which included completeness of treatment records, availability of HIV status and disease stage, etc It is possible that a number of HIV positive SAM cases at Holy Cross hospital were excluded from the study, for example on account of having incomplete records, resulting in fewer cases in this group at the same hospital. Furthermore, the total number of SAM cases included in the analysis was 454, of which 144 (32%) were from St Patricks hospital and 310 (68.3%) from Holy Cross Hospital. More cases were obtained at Holy Cross hospital as the duration of data collection in that facility was much longer compared to St Patricks Hospital. At Holy Cross hospital, data collection using patient treatment records was conducted until the end of phase 3 of the study (53rd month). At St Patrick's hospital, however, this process stopped after the 32nd month. This was due to internal bureaucratic dynamics at the time, which prohibited access to patient records by outsiders. This therefore begs the question as to whether the SAM cases unaccounted for in the remainder of the study period at St Patrick's hospital may have shifted the proportions to a certain degree.

The similarities in the distribution of clinical characteristics other than HIV status on admission may be accounted for by the fact that the population served by each hospital is almost the same in many respects (Puoane et al., 2006). Even though the two hospitals are about 100 km apart, and supposedly responsible for serving a specific catchment area, the social determinants of health are comparable (Municipal Demarcation Board, 2008). Therefore, the health status in these two areas is likely to be similar, particularly the prevalence of undernutrition and associated co-morbidities.

This was evident during the qualitative enquiry. Participants from each facility shared similar views regarding the social-cultural determinants of some observed clinical characteristics of SAM on admission. The most striking clinical characteristic was severity of SAM on admission which was attributed to sociocultural dynamics at household level.

The similarities between the two hospitals in terms of the CFR are however more complex to explain. The FGDs held in each hospital revealed that there is a web of factors which contribute to higher CFRs. These factors manifest at the leadership levels within the broader health care system, the community and the hospital in which the management of SAM cases takes place. They range from the antecedents of critical illness such as traditional medical use and household negligence, to high HIV prevalence associated with lack of status disclosure and poor adherence to ART which result in virological failure, misdiagnosis at the first point of care, and lack of hospital-level expertise to deal with complex presentations, as well as sporadic lacunae in the skilled workforce and resources to sustain the quality of care.

Figure 38 provides a framework which describes some system-wide factors believed by interviewed health care workers to contribute to high case fatality rates in both hospitals. Most of these factors (traditional medical use and household negligence, misdiagnosis at the first point of care, lack of hospital-level expertise to deal with complex presentations, as well as sporadic shortages in the skilled workforce and resources to sustain the quality of care), were also observed as part of the ethnographic enquiry. Herbal intoxication was used as an indicator of traditional medicine use and was categorised as "other comorbidity" in Phase 2 of the study.

The dark-shaded areas indicate some proximal risk factors for high CFRs observed at the study sites during the ethnographic phase of the study. Interestingly, these were also perceived by the health care workers to have a more immediate effect on high CFRs at facility level. The factors in the unshaded boxes are more distal and most likely to be beyond immediate control of the health care worker.

Perhaps what was not highlighted during focus group interviews with the health care workers is the failure of the clinical team at each hospital to diagnose and treat TB. Tuberculosis has been identified in a previous study as an important SAM comorbidity that is associated with high CFRs (DeMaayer and Sallojee, 2011). In the current study, only very few cases were confirmed to have TB which is less likely considering the fact that TB is often comorbid with HIV and other LRTIs (Heikens, 2007),

The second hypothesis stated that there would be no statistically significant difference between HIV infected and uninfected SAM cases with regards to syndromic classification of SAM. The analysis showed that more HIV positive SAM cases were marasmic compared to their HIV negative counterparts and that fewer were cases with Kwashiorkor. These findings do not support the stated hypothesis. However they corroborate the evidence from similar studies conducted elsewhere in Africa (Prazuck et al., 1993; Kessler et al., 2000).

Prazuck et al. (1993) and Kessler et al. (2000) have also demonstrated that HIV infection was associated with marasmus. While it is usual to present with Kwashiorkor in the region where the study was conducted, with HIV infection, the illness itself results in wasting due to changes in physiological and metabolic functions (Mehta et al. 2013).

The current study also tested the hypothesis that there would be no statistically significant differences between the two hospitals in terms of survival of SAM cases if no other clinical characteristics – including HIV status - were considered in the analyses. Based on the results from the Kaplan Meier Failure Curves and the log rank test for equality of failure functions, this hypothesis was supported. There were small and statistically insignificant differences between the two facilities in terms of survival prospects, even though Holy Cross hospital performed slightly worse than St Patrick's.

When HIV status was considered, the same statistically insignificant differences in the pattern of survival between the hospitals were also detected. The small differences between Holy Cross hospital and St Patrick's hospital in terms of the relative survival prospects of HIV infected and uninfected SAM cases were not statistically significant. In both hospitals, HIV infected SAM cases died in larger proportions than their HIV uninfected counterparts.

The small differences in survival between the two hospitals mirror the corresponding quality of care also measured as part of this study phase. It was noted that St Patrick's hospital generally scored better on various quality-of-care indicators

than Holy Cross hospital. However, although it makes logical sense to postulate that the higher the quality of care the better will be the survival probability, it is the researcher's view that the relationship between survival and quality of care in the context of the current the study should be considered with caution. The measurement of quality of care was not objective enough even though the researcher used widely used and traditional quality of care measurement techniques (Donabedian, A. 1988) in the study to assess the extent to which SAM cases were treated as was required. During the ethnographic enquiry the assessment of quality of care was more objective. However, in the absence of the researcher, quality of care was documented and the researcher was only able to assess how well treatment was done based on the notes written down by health care providers. As described in the methods section, some measures were put in place to curtail this measurement bias but this may not have been sufficient to address issues of data completeness, correctness, accuracy, consistency, and appropriateness. It is possible that the information collected over time from different cases may have been measured and recorded by multiple individuals with varying professional attributes, thereby introducing some inconsistencies in the validity of the measurements. This kind of threat to data validity has been documented before in similar study designs (Thiru, Hassey and Sullivan, 2003). A much more elaborate discussion around the quality of care is provided at the end of this section.

The pooled analysis revealed that CFR differed between HIV infected (41%) and HIV uninfected SAM cases (11%) that were part of the revised intervention. The estimates in the current study were slightly higher than those reported in a recent and similar

study conducted in Burkina Faso, in which the CFR among HIV infected SAM cases was 39.7% and 10.9% among their HIV uninfected counterparts (Savadogo et al, 2013). A study in Niger (Madec et al, 2011) also reported the same direction of relationship but with much lower CFRs for HIV infected SAM cases and uninfected SAM cases (20% and 14% respectively) compared to the current study.

The differences in levels of CFRs between the current study and the other two studies may be explained by the fact that unlike the current study, which used a purposeful sample, the study in Niger used prevalence data collected on a much larger scale. The current study was therefore more likely to suffer from selection bias. The selection bias may, for example, be a result of the fact that only SAM cases that had complete hospital records which provided insight into the variables of interest and which were drawn from only two hospitals, were selected into the study.

In a study by Puoane et al (2008), a comparative analysis of the CFRs from the two hospitals involved in the current study showed that CFRs for SAM had decreased from above 30% in 1999 to below 10% by the year 2004 following a training intervention. This was an encouraging achievement considering the target CFR of less than 15% specified by the WHO as the threshold for classifying SAM - related fatalities as a public health problem. What the study by Puoane et al (2008) did not take into account, which was demonstrated in the current study, was the disaggregation of CFRs by HIV status. The current study revealed a combined CFR of 25% over a period of 4 years (2009 - 2013). However, the CFR among HIV negative SAM cases (i.e. 11%) was well below the WHO cut-off point of 15%. This

was unlike the CFR for HIV infected SAM cases which was 41%. Unfortunately, there is currently no consensus agreement as to what the cut-off point should be in respect of the CRF among SAM cases who are HIV infected. As will be shown later in this chapter, the longitudinal analysis of CFR from 2009 to 2014 showed that CFRs attributable to SAM and HIV decreased to about 6% (60 deaths per 1000 admissions) by 2014. However, this result was based on smoothed analysis of monthly data and therefore does not account for fluctuations in CFRs that occurred during the entire assessment period. Nevertheless this finding demonstrates an improvement in treatment outcomes in the current study design compared to its predecessor which was initiated in 1999 by Puoane et al (2008).

The CFRs reported in this study can be directly linked to disease severity on admission, which is itself a possible result of several factors illustrated in Figure 38. However, not all the factors illustrated in this Figure as antecedents of case severity apply to both HIV infected and uninfected SAM cases. For example, while virological failure at admission for neglected SAM cases may be the most critical antecedent of case severity among HIV infected SAM cases, herbal intoxication may predominantly precede case severity among HIV uninfected SAM cases. Other factors associated with high case fatality rates, which have been documented before (WHO, 2013) and were demonstrated in the current study include multiple concurrent infections, shortages of medical supplies, and inadequately skilled health workforce. As will be discussed in Chapter 10, these are some of the areas which need immediate attention.

Perhaps what the current study adds to the body of knowledge is the pattern of survival among HIV infected SAM cases that were at different stages of HIV infection. Contrary to the hypothesis, the study was able to show that survival prospects differed across the four HIV disease stages and that it worsened with later stages of HIV infection. The Kaplan Meier failure curves and the Cox regression analyses revealed that the real threshold for higher risk of death was when cases were admitted at Stage 3, followed by Stage 4.

The reasons for excess mortality risk associated with advanced stages of HIV infections in SAM are not yet well documented particularly in the context of ART (Ndekha, et al. 2004). However, some authors continue to attribute excess mortality to complex pathophysiological, metabolic, and pharmacological changes that occur as HIV infection progresses (Savadogo, et al. 2013). HIV infected SAM cases in the current study were initiated on ART as appropriate using the treatment guidelines described in section 4.6.3.4. This is in spite of the fact that the timing of ART in preventing premature mortality among HIV infected SAM cases at different disease stages remains a challenge. A randomised controlled trial has shown that half the children hospitalised for SAM developed oedema after starting ART (Prendergast, et al. 2011). In the same study, one in 14 children who were at an advanced stage of HIV infection became oedematous 12 weeks after ART initiation. The current and other studies have shown that kwashiorkor is less common than marasmus in HIV-infected children (Bachou, et al. 2006; Amadi, et al. 2001). The development of oedema following ART initiation may contribute to poor rate of weight gain among SAM cases with advanced HIV infection. This is probably linked to an Immune

Reconstitution Inflammatory Syndrome (IRIS) which has been shown to have an association with the development of oedema in other studies (Bower, et al. 2005).

The findings from this study regarding severity of illness on admission and survival probability are consistent with past evidence by Maitland et al (2006), but do not support the hypothesis stated at the beginning of this study. Severely ill SAM cases, that is, those admitted with one or a combination of clinical features such as coma, hypoglycaemia, hypothermia and bradycardia as shown in Table 2; had the worst survival probability compared to those who had other less severe SAM-related manifestations such as herbal intoxication, cushingoid facies etc.

These findings may have important practice implications. As Maitland et al (2006) have argued, the clinical features associated with higher risk of death can be used by front-line health care givers to target emergency treatment and allocate resources more appropriately. This is particularly important in the context of poor human and material resources in most rural hospitals in Sub-Saharan Africa, including the ones in which the current study was conducted. It was also interesting to learn that most health care workers who were interviewed during the FGDs believed that the effectiveness of the WHO guidelines depended on the severity of the case. This statement supports another view from the doctors that, there is often a lack of specialist physicians to handle complex presentations. The role of macro-level policy processes to ensure that under-resourced facilities have access to specialist clinicians, in addition to the required medical resources and infrastructure to optimise treatment outcome, becomes crucial. However, with mortality being highest in the first 2 hours of admission there is a need to institute proper and well supported and

sustained triage and emergency management mechanisms so that not only are the "at-higher-risk-of-death" cases identified but treated according to the guidelines available. Continued attention to appropriate diagnosis of common complications such as TB and Urinary Tract Infections also need to be prioritised as these do not always require a specialist physician and can be managed by most professional nurses in South Africa with minimal supervision by a physician.

The multivariate Cox proportional hazard model revealed that age, SAM syndromic classifications, oedema and dermatosis grades on admission, some forms of SAM comorbidities, as well as Stages 1 and 2 of HIV infection were not associated with mortality among SAM cases in this study. The adjusted model showed that only case severity, the presence of LRTIs and advanced stages of HIV infection were associated with higher mortality. TB was less common among participants included in the current study compared with LRTIs. This is probably because TB is difficult to diagnose microbiologically and some researchers have documented its treatment based on clinical suspicion (DeMaayer and Sallojee, 2011). Therefore, it is possible that some cases that had TB were missed in the current study despite TB being an important comorbidity in the management of SAM in the context of HIV infection. Nevertheless, the excess mortality attributable to LRTIs highlights the importance of effectively treating infections in SAM. A review of some treatment records showed that there have been few instances of incorrect drug administration, irregular dosing and provision of the wrong dose, particularly considering the fact that the skilled health work force was not stable throughout the study period. This was despite all the measures put in place to mitigate this shortcoming.

A study by Koethe and Heimburger (2010) has shown that SAM, immune function and infection burden interact in children, particularly in the context of HIV infection. This was also evident during further analyses conducted as part of this study to assess the synergistic effect of factors identified in the multivariate Cox proportional hazard model as significant predictors of mortality among SAM cases. Being critically ill and having LRTI's were, both independently and as a combination, potential effect modifiers of the higher risk of death as they increased the hazard of death quite substantially when they were combined with HIV infection in the interaction model.

This finding therefore refutes the null hypothesis that being critically ill on admission, having HIV co-infection and/or LRTIs comorbidity are not statistically significant effect modifiers of higher risk of death among SAM cases. Savadogo et al (2013) have also argued that multiple infections and metabolic complications have synergistic effects on mortality in SAM, more so when HIV infection is involved.

It is important to discuss the above findings in light of the study intervention. This study involved a structured intervention which, if implemented correctly and adequately, was able to contribute to improved treatment outcomes. Most quantitative studies conducted in the past within the context of the WHO guidelines have not reported on the quantitative relationship between treatment outcomes and the quality of clinical care. The study by Ashworth et al. (2004) is perhaps one of a few which have attempted to show this relationship. Other authors, including Karaolis et al. (2007) and Puoane et al. (2004) have qualitatively assessed the aspect of quality of clinical care as it relates to the implementation of the WHO guidelines.

The current study investigated the relationship between processes of care as posited in the WHO guidelines and mortality using a quantitative approach. This study therefore adds a new dimension to the body of knowledge as it attempted to show, in statistical terms, how much the quality of clinical care provided to SAM cases using the WHO treatment guidelines determined their hazard of death. The un-exponentiated adjusted Cox regression model coefficient for the quality of care revealed that for every one unit increase in the composite score of quality of care, the hazard of death dropped by 24%. Although the current study design was not as rigorous as a randomised controlled trial, this finding is worth considering in light of the effectiveness of the WHO 10-step treatment guidelines. The implication of this finding is that if the WHO guidelines are implemented fully and correctly, the likelihood of survival will be increased. This relationship has also been demonstrated in another study which used a different study design (Ashworth et al., 2004). However, their enquiry had a limitation. The analyses did not consider the relationship between mortality hazard and the quality of clinical care in terms of HIV status.

Stratifying the analysis by HIV status using the principle component analysis approach was however beyond the scope of the current study. The current study therefore fails to show whether the findings regarding SAM and HIV comorbidity were confounded by inadequate management of HIV disease itself. Future research should therefore consider assessing whether there is a differential response to the quality of clinical care based on the WHO treatment guidelines by comparing HIV infected and uninfected SAM cases. A much more robust study design such as a

randomised controlled trial should be used to ensure that the inferences made are much more accurate.

The quantitative approach used to appraise quality of clinical care had some limitations which should also be considered. Some authors have argued that even though clinical records are the source documents for most studies on medical care processes, they can sometimes be sketchy or report inaccurate information about the treatment process and outcomes thereof (Clute, 1963). Besides the challenges relating to the veracity and completeness of the information in the treatment records, observer error may also occur under the best of circumstances (Kilpatrick, 1963). Therefore, it becomes essential to ensure that a verification process is adopted as part of the assessment of the care process.

In the current study, standard operating procedures (SOPs) were put in place to implement the intervention as it was planned and to improve the validity of the data recorded in the patient's clinical records. The measurement tools and information recording processes were standardised. A peer-verification process was also followed during data collection to ensure that the information being evaluated was as accurate as possible. This was in addition to ensuring that the WHO guidelines are implemented as intended.

Despite these efforts however, there may have been some measurement inconsistencies over the course of the study. This is particularly possible considering the fact that some health care workers who were not yet trained on how to follow the study SOPs were involved in recording diagnostic and treatment

information. Furthermore, the quantitative assessment of the extent to which the guidelines were implemented revealed some gaps, particularly at Holy Cross hospital. Although these shortfalls can be considered minimal, the findings relating to the relationship between the quality of care and treatment outcomes in this study should be considered conservatively.

9.3. PHASE TWO - PART TWO: Rate of weight gain, duration of hospitalisation and HIV infection in the context of the WHO "10-steps" treatment guidelines

The second part of Phase 2 tested two main null hypotheses. The first hypothesis stated that the rate of weight gain and the duration of hospitalisation among SAM cases would not be different based on HIV status and disease stage, both *within* and *between* the two hospitals. The between-hospital comparison of the median rate of weight gain without stratification by HIV status showed no statistically significant differences. However, this was not the case with regards to the duration of hospitalisation. The median duration of hospitalisation for discharged cases, regardless of their HIV status, was higher at St Patrick's hospital.

The similar median rates of weight gain between the two facilities are somewhat surprising and difficult to explain. This is particularly so considering the differences observed between the two facilities in respect of the quality of clinical care. However, the higher median duration of hospitalisation at St Patrick's hospital can be explained in two ways. The ethnographic enquiry revealed that St Patrick's hospital was much less burdened by the patient load than Holy Cross hospital. At

the latter hospital, the paediatric ward tends to be full most of the days. The resultant shortage of beds necessitates premature discharges. This ethnographic observation was also corroborated by the findings from a FGD held with frontline health care givers. A nurse at Holy Cross hospital mentioned that if the child has got appetite they are discharged to free up the space for incoming admissions. And yet, in both the revised and old interventions, eating well is only one of 6 criteria that should be fulfilled before a child can be discharged. Although premature discharge of SAM cases was also observed at St Patrick's hospital, this occurred less frequently.

These findings highlight the difficulty involved in observing the treatment protocol when faced with structural challenges beyond the control of a health care worker. Unfortunately, structural challenges were not sufficiently tackled in the revised intervention. Future interventions should therefore consider macro-level factors which influence clinical care. Improving the physical infrastructure of the hospital - such as expanding ward space and increasing the number of beds - and ensuring more effective and sustainable resource mobilisation to close the gap in availability of medication and formula feeds, would be some of the crucial steps towards addressing the issue of premature discharge. Furthermore, ensuring that the discharge criteria are observed and sustained will be crucial. An interesting finding that emerged from the FGD was that one head of nursing reported that there were guidelines which indicated that children should not be kept longer than 5 days in the hospital. This seemed to be a misguided view as there are no such guidelines currently available in South Africa.

The comparison of HIV infected and uninfected SAM cases in terms of their rate of weight gain and duration of hospitalisation revealed some findings which both agree and disagree with the current literature. When data from both facilities were combined, the median rate of weight gain among children who survived was 7.5 g/kg/day for HIV uninfected SAM cases and 3.6g/kg/day for their HIV infected counterparts. This was an encouraging finding considering the context within which nutritional rehabilitation occurred. The same direction of the results was found in each hospital when the data were disaggregated by facility. However, Holy Cross hospital recorded much smaller medians for both groups than St Patrick's hospital.

This difference may again be considered in light of the differences in the quality of care measured between the two facilities. More specifically, the ethnographic observations revealed that the frequency of feeding, accuracy in making formula feeds and mealtime supervisions were much better at St Patrick's hospital than at Holy Cross hospital. However, the quantitative evaluation of these aspects based on patient records revealed somewhat marginal differences.

Savadogo et al. (2013) also found similar relationships even though their intervention achieved much faster median rates of weight gain. Severely malnourished cases with HIV infection achieved a median of 4.64g/kg/day versus 9.04g/kg/day for SAM cases without HIV infection. On the contrary, Fergusson et al. (2009) reported similar rates of weight gain between HIV infected and uninfected SAM cases (mean = 8.0 vs 8.9 g/kg/day, respectively). The findings by Fergusson and colleagues are however surprising given the number of several other studies which have also shown that nutritional recovery is much slower in HIV infected

SAM cases than in their HIV uninfected counterparts (Ticklay et al., 1997, Ndekha et al., 2004; Sandinge et al., 2004).

In the current study, the poorer nutritional recovery observed among HIV infected SAM cases may, in part, be a result of metabolic changes associated with HIV infection which impact on the nutritional status of the child. These changes include for example hyper-metabolism of energy stores, nutrient losses and malabsorption as a result of illnesses of the gastrointestinal tract, reduced bioavailability of certain nutrients, and altered nutrient utilisation (Mehta et al., 2013). Poor appetite resulting in inadequate nutrient intake has also been documented (WHO, 2013). Cases with HIV infection tend to present with severe oral and oesophageal candidiasis which undermine therapeutic feeding efforts (Trehan et al. 2012).

The study also showed that the rate of weight gain becomes poor with advanced HIV disease stages. This finding can be accounted for in light of the randomised controlled trial by Prendergast, et al. (2011) which demonstrated that half the children hospitalised for SAM developed oedema after starting ART. Oedema may be associated with a slower rate of weight gain as children with oedema have to firstly lose weight during the rehabilitation phase before they gain non-oedema-associated weight. Another possible explanation for this is that oedematous children are often sicker and unable to adequately metabolise nutrients. The evidence around this physiologic process is nevertheless still poorly documented. However, the fact that ARVs may increase the incidence of oedema necessitates a scientific enquiry into the potential role of ART in slowing down the rate of weight gain in SAM.

With regard to the duration of hospitalisation, the pooled analysis showed no differences between HIV infected and uninfected cases (Median=12 days in both groups). When the data were disaggregated by hospital however, St Patrick's hospital generally recorded longer durations compared to Holy Cross hospital. The duration of hospitalisation was only considered for cases that were discharged. The inclusion of cases that died would have introduced some systematic errors in the analysis as some of them died before the third day of hospitalisation.

The finding about duration of hospitalisation in relation to HIV status conflicts with results from a recent study by Madec et al (2011). Although Madec and colleagues used a different statistical estimate, their study showed that the duration of "re-nutrition" was much longer among HIV infected cases (Mean = 22 days) than in HIV uninfected cases (Mean = 12 days).

The difference between the two studies is not surprising, however. In the current study, the duration of stay in the hospital depended on factors other than nutritional recovery, including availability of beds as mentioned earlier. On the contrary, SAM cases in the study by Madec and colleagues were allowed to be on hospital treatment until they recovered well or died. Their intensive phase of re-nutrition lasted a minimum of three weeks. Their findings seem to imply that the minimum number of days required to achieve good nutritional recovery is roughly 22 for HIV infected SAM cases and 12 for HIV negative cases. However, neither the current study nor Madec's were able to provide precise quantifiable targets such as time taken to achieve weight for height Z-scores, which are oedema-free.

The current study also attempted to show the relationship between the mean rates of weight gain and the duration of hospitalisation by HIV status. The working hypothesis was that there would be no differences in the mean rates of weight gain between HIV infected and uninfected SAM cases at different time intervals. Therefore the analysis focused on mean rates of weight gain calculated on a sample of SAM cases that were discharged within specific intervals.

The analysis showed that this hypothesis was not supported. The mean rates of weight gain were consistently higher among HIV uninfected than HIV infected SAM cases at different time intervals. It was also noted that in both groups, those who gained weight more rapidly were able to be discharged sooner (i.e. between the 6- to 14-day window). Cases whose weight increased more slowly stayed longer in the hospital. Also, SAM cases that were discharged before the 5th day of hospitalisation achieved a slower rate of weight gain during the post stabilisation phase. This is possibly because these cases were not long on F100. These results corroborate the fact that the rate of weight gain is a function of both the dietary intake and the number of days spent taking the feeds.

9.4. PHASE THREE: Sustainability assessment of the revised intervention

The interrupted time series study design has been widely documented as a powerful quasi-experimental design which can be used to evaluate the effects of interventions when random assignments are not feasible (Taljaard et al., 2014; Shadish et al., 2002; Gillings et al., 1981). The power of this design lies in the fact that it has the ability to distinguish the effect of the intervention from secular changes which would have

happened in the absence of the intervention (Taljaard et al., 2014). However, this type of impact evaluation design has not been applied to assess the effects of discontinuing an intervention - as opposed to introducing it - on the sustainability of the gains realised during the intervention period.

During the current study, the researcher used an interrupted time series design with a removed intervention approach. The latter has been shown by Shadish, Cook and Campbell (2004) to have the ability to show that the outcome improves and worsens with the presence or absence of the intervention. To the researcher's knowledge, the current study is the first of its kind to use this design to evaluate the sustainability of a hospital-based nutrition rehabilitation intervention to improve the management of SAM.

Three main null hypotheses were tested as part of this study phase. Firstly, the study tested the hypothesis that in both hospitals there would be no statistically significant month-to-month decrease in mortality related to SAM before discontinuing the intervention. The study showed that in both hospitals, there was a trend (slope) of a decrease in mortality related to all three performance metrics (Total SAM deaths, SAM deaths within 24 hours of admission, and deaths attributable to SAM and HIV) during the period in which the intervention was active. However, these changes were not statistically significant.

It is less likely that the lack of statistical significance was attributable to the number of data points used to estimate the effects. There is evidence to show that the minimum number of data points required to detect the effect is 12 before and after

series interruption - in this case the discontinuation of the intervention (Ramsay et al., 2003). The current study involved 69 data points in total, 32 of which were used in the pre-intervention discontinuation segment and 37 in the segment following the discontinuation. It is therefore possible that indeed mortality trends did decline during this period in both hospitals, but not to a level that would have shown statistical significance. Despite the lack of statistical significance, however, this decline demonstrates the effort of the hospitals and the intervention to improve mortality related to SAM during the intervention period.

The line plots for the observed monthly mortality rates for all three performance metrics showed that there were some outliers in the time series data. This was one reason why a model-predicted line plot was used to smooth the data. Some researchers have suggested that quarterly data points give reasonable time intervals for model estimation when there are outliers or significant variations in consecutive time series data (Ramsay et al, 2003). This approach was nevertheless not considered in this study as quarterly statistics on mortality would have undermined month-to-month changes that were central to the objective of the revised intervention.

Before the beginning of Phase 3 of the study, it was also assumed that there would be no statistically significant trend increase in the three metrics following the discontinuation of the revised intervention. Based on this hypothesis, a statistically significant trend increase in any of the three metrics during this period meant that the intervention was not sustainable.

The model-predicted line plots for the period following the discontinuation of the intervention showed that there was a statistically significant trend increase associated with total monthly SAM mortality at Holy Cross hospital. At St Patrick's hospital, the model predicted line plots showed a slight decrease in the same period. These findings imply that the intervention was not sustainable on this metric at Holy Cross Hospital unlike at St Patrick's hospital.

The differences between the two hospitals may be difficult to account for. Taljaard et al. (2014) have noted some challenges associated with using interrupted time series to evaluate complex quality improvement interventions. Sometimes there may be some components related to the intervention which are introduced or removed at different time points. In the current study for example, there may have been some historical events which occurred specifically at Holy Cross hospital after the intervention was discontinued, leading to the worsening of the hospital's performance on this metric. Such events may have included chronic shortage of the health workforce or shortage of medical supplies amongst other things.

During the fourth Phase of the study, an attempt was made to explore some of the reasons why mortality attributable to SAM increased significantly at Holy Cross hospital following the discontinuation of the intervention. However, the reasons which emerged during FGDs were general and therefore could not be linked specifically to these findings as potential threats to the quality of care. An ethnographic enquiry could possibly have provided much more accurate insights into these dynamics. However, this part of the study ended at the same time the intervention was discontinued.

During data analysis, it was also noted that there were some outlying monthly mortality data which may have shifted the slope of the regression segments. Sensitivity analyses, censoring of outliers and Autoregressive Integrated Moving Averages (ARIMA) modelling are some of the methods that could have helped alleviate the validity threat to the time series model. However, the use of these methods was beyond the scope of this investigation.

The most notable result from this part of the study was the sustainable reduction of mortality attributable to SAM and HIV as well as SAM deaths within 24 hours in both hospitals after the intervention was discontinued (Figure 36 and 37). The hypothesis that there would be no statistically significant trend increase in mortality attributable to these two performance metrics after the discontinuation of the intervention was therefore supported by the data. Even though these reductions in mortality over time were negligible and not statistically significant, the efforts made by the hospitals to sustain the outcomes realised during the intervention period should not be ignored.

Equally worthy of note is the fact that the baseline levels for these two metrics were higher than the end point levels. The baseline level for death within 24 hours changed from 100 to 70 deaths per 1000 cases, and from 120 to 40 deaths per 1000 cases at Holy Cross hospital and St Patrick's hospital, respectively. Similarly, the baseline level for death attributable to HIV and SAM changed from 100 to 60 deaths per 1000 cases, and from 95 to 60 deaths per 1000 cases at Holy Cross hospital and St Patrick's hospital, respectively. This demonstrates a shift possibly brought about by the intervention during the study period.

The current study was framed and conducted using the principles of operations research and theory driven enquiry. Within the context of operations research, the study was initiated with the identification of the problem and the development of the solution which was implemented and evaluated. The development of the solution – the revised intervention - was theory-driven and took into account all possible inputs and processes that would lead to better SAM treatment outcomes within the study setting. Furthermore, all possible moderating factors which may promote or hinder the translation of inputs and processes into the desired outcomes and impacts were infused in the study as a point of enquiry post the implementation phase.

9.5 Main contributions of the current study to the existing body of knowledge

The current study has both corroborated and added new knowledge to the existing body of literature around the epidemiology and management of SAM in the context of HIV infection and the WHO ten step treatment modality.

The most outstanding new contribution to the body of knowledge is that in the current study it was shown that HIV disease stages have differential impact on treatment outcomes in the context of the current WHO treatment guidelines for management of SAM cases with HIV infection. Compared to earlier stages of HIV infection, survival was poorer for HIV positive SAM cases that were at stage 3 and 4 at admission. The risk of death was highest for Stages 3 and 4 of HIV infection. Furthermore, the study showed that the median rate of weight gain got smaller with advanced HIV disease stage, whereas the median duration of hospitalisation became

larger. What adds value to these findings is the fact that generally there were no significant differences between the two study hospitals in terms of the patterns of survival and clinical manifestations among SAM cases who were admitted

The study also generated some relatively new knowledge around the impact of severity of SAM and HIV comorbidity on treatment outcomes. Both these factors were the strongest independent predictors of death among SAM cases, both in the adjusted and unadjusted models. Also, being critically ill and having LRTI's were, both independently and as a combination, potential effect modifiers of higher risk of death as they increased the hazard of death quite substantially when they were combined with HIV infection in the interaction Cox regression model.

The current study also used a new statistical technique to assess the relationship between the rate of weight gain and duration of hospitalisation which has not been demonstrated before. Results from this analysis showed that HIV negative SAM cases consistently attained much faster mean rates of weight gain than their HIV negative counterparts within the same time interval. The mean rate of weight gain was much faster during the first few days following the stabilisation phase for both HIV positive and HIV negative cases, but levelled out almost after the 14th day following the stabilisation phase.

Furthermore, this study was the first of its kind to assess the impact of discontinuing a nutrition rehabilitation programme at facility level on SAM treatment outcomes using an interrupted times series design and Poisson segmented regression modelling. First of the study showed that Poisson segmented regression modelling

can be applied on interrupted time series data collected as part of a facility-based nutrition rehabilitation intervention to detect level and trend changes in treatment outcomes related to SAM over time. Based on this method, the study showed that the intervention was sustainable in improving three mortality indicators of SAM after the intervention was discontinued. However, the total SAM mortality worsened every month after the discontinuation of the intervention at Holy Cross hospital, indicating that the programme was not sustainable for this metric.

Lastly, through the ethnographic enquiry and discussions with health care workers at both facilities, it was noted that the implementation of the WHO treatment guidelines within under-resources settings may not always be optimal even under external support initiated by researchers. There are factors beyond the control of the hospital management structures and health care teams which curtail full implementation of the guidelines. To a large extent, these include for example, lack of policy commitment at macro-level to ensure effective and sustainable supply of the necessary material and human resources to meet minimum requirements for the implementation of the guidelines, at facility level, there are constant rotations of health care workers from ward to ward which results in gaps in the skilled health workforce able to effectively treat SAM cases. Furthermore, there are weak procurement mechanisms in rural hospitals which create a huge demand and supply gap in terms of medication and other indispensable resources required for effective treatment and management of SAM.

Furthermore, there are some community-based social dynamics that make the implementation of the guidelines even more difficult within resource-limited

settings. These include for example poor health-seeking behaviour whereby parents bring their children/infants for treatment of SAM at a later stage or with other complications arising from traditional medicine practice which are not catered for in the WHO guidelines and not always easy to treat as a result of untrained health care workers.

9.6. Generalisability of the study findings

The current study was conducted within a rural setting. Even though the researcher used two hospitals to increase the generalisability of the findings to similar facilities, it is his view that if the study was to be conducted in other facilities within the same geographical setting, the results may not necessarily be similar. This is particularly the case in respect of clinical outcomes as these are affected by a web of factors both within and beyond the facility which may not manifest with similar intensity across all facilities in rural sites. However, with regards to the epidemiology of SAM in the context of HIV infection and other comorbidities prior to treatment, the findings of this study can be generalised within the same province but not necessarily beyond. This is primarily because the social determinants of health have been shown to be similar across the entire province as has been discussed earlier.

CHAPTER 10

CONCLUSION AND RECOMMENDATIONS

10.1. Conclusion

The findings from this study are largely consistent with what other studies have shown in the past with regard to SAM in the context of HIV infection, before and after initiating treatment using the WHO treatment guidelines. This was particularly the case in respect of survival and nutritional recovery. The role of HIV infection in excess mortality among children treated for SAM using the WHO guidelines was evident in this study. The study Also demonstrated that survival prospects and the rate of weight gain differ significantly depending on the stage of HIV infection. The study also revealed that case severity, multiple concurrent infections and HIV infection have a synergistic effect on excess mortality among children treated for SAM using the WHO treatment guidelines. This interactive effect of multiple risk factors has also not been adequately documented in the literature around SAM.

Another new finding which came out of this study was that segmented Poisson regression modelling can be applied to interrupted time series data to assess the sustainability of a facility-based nutrition rehabilitation intervention. Although the ethnographic phase of the current study was relatively less objective, it revealed that the management of SAM in the study settings is affected by a web of factors which manifest at community level, the facility and the broader health care system.

10.2. Recommendations

The high prevalence rate of HIV infection in the study population and the resultant treatment outcomes lend support to the notion that the WHO treatment guidelines should be revised to ensure that mechanisms for effective treatment of HIV

comorbidity in SAM are in place. The revisions ought to tap into the differential energy requirements by HIV status, timing of ART initiation among HIV infected SAM cases as well as developing a broad-based triage system to more effectively identify and treat SAM cases that are at higher risk of early death. Even though the current study has generated some further insights into the required evidence, there is a need for large scale and rigorous studies to inform these decisions. Further studies also need to tap into the most effective ways of diagnosing TB in children with SAM in resource limited settings so that it can be treated and possibly alleviate its potential contribution to the observed high case fatality rates in the study setting.

The role of the broader health care system in South Africa in preventing incidences of SAM at community level in the study setting is discernible. The current study has shown that the admission rates attributable to SAM at both hospitals remains high and as such requires mitigation. Community-based prevention strategies developed through multi-sectoral engagements have a huge role to play in achieving this goal. It goes without saying that early detection of SAM would be a crucial part in preventing disease severity and the development of multiple infections, thereby reducing the likelihood of subsequent preventable death associated with SAM in the study setting.

For children who develop SAM at community level, well supported community-based nutrition rehabilitation programmes may play a huge role in alleviating the challenges associated with facility-based care such as patient load, lack of resources, amongst other thing. With the current drive to re-engineer primary health care in South Africa, this recommendation would be worthwhile to consider. However, it

would be important to ensure that there are effective referral networks which link community-based therapeutic centres and the formal health care facilities, to ensure that cases that have complications and require special attention are treated appropriately. This is particularly important considering the fact that case severity on admission was the leading predictor of mortality in the current study.

Community-based health workers can be identified and trained to take up this role. They may also be involved in efforts to integrate traditional medicine with the conventional health care system as recommended by the WHO. This may eventually reduce the number of SAM cases with concurrent herbal intoxication which were received on an ongoing basis during the study period. Community-based health workers may also have a huge role to play in alleviating the challenge of delayed care resulting from gross negligence by the mother or the primary care giver of the child as were the cases in the current study. However, there is a need for future qualitative studies to explore further the health-seeking behaviour of HIV positive mothers in the study and/or similar setting, whose children are prone to or have SAM, to understand their knowledge, attitudes and practices regarding health care so that better informed interventions can be developed. It is the researcher's view that the information that was generated from the FGD with health care workers doesn't not constitute the absence of additional evidences in to systemic factors which contribute to SAM case severity. The findings presented in Figure 38 therefore need to be supplemented and substantiated in further studies.

Given the challenges reported in this and many other studies in respect of shortages of the health care personnel who are trained in the management of SAM, the need

for curriculum infusion in the formal nursing and medical education system in South Africa is crucial. This is one recommendation which should be actualised soon enough. This is important considering the fact that there is a concurrent policy in most rural hospitals which mandates fr0nt line health care givers to rotate through different wards as part of the skills development initiative. This was observed in the current study. It is therefore important that nurses who undergo the clinical rotation within the paediatric ward have the pre-clinical co-competencies on how to effectively manage cases with SAM using standardised guidelines.

The issue of sporadic shortages of medical and other therapeutic supplies which was shown in the current study has been also been documented in a number of studies conducted in South Africa. The initiation of district clinical specialist teams (DCSTs) in South Africa holds promise in ensuring that there are sustainable structures in place to identifying specific operational issues within the health care system in the country. There is a need to scale up this initiative in rural areas where the deployment of DCSTs remains poor. Their mandate in conducting operations research and developing solutions as appropriate has a huge role in improving leadership and accountability within the health care infrastructure.

The close linkage between SAM and HIV/AIDS begs an integrated health care approach to ensure that hospitals and HIV clinics work in harmony to optimise outcomes both for the child and the mother.

10.3. Strength of the study

The use of the explanatory mixed methods approach in this study provided a better understanding of the quantitative findings within the context of the intervention. For example, the qualitative enquiry helped the researcher to interrogate some of the antecedents of case severity for SAM on admission as well as some facility-specific and system-wide factors which may contribute to high CFR in the hospital. Understanding the dynamics of case severity and the resultant high case fatality rates from a contextual perspective provide a platform for developing well informed interventions which can address the problem at issue more effectively.

The two sub-studies of Phase 1 used a study sample which was larger than that calculated for the study. This made it possible to conduct further analysis using multiple variables, including the principle component analysis technique to assess the quality of clinical care, as well as interaction modelling to estimate the synergistic effect of multiple risk factors on excess mortality risk.

The strength of this study also lies in the use of clearly predefined exposure and predictor variables as well as the confounders and effect modifiers. These were guided by the research problem as well as the literature and thus respond to the current knowledge gaps.

Furthermore, as mentioned in Chapter 3, a number of measures were instituted to ensure that the data used during analyse were valid and reliable. The use of SOPs in this study is also one strength which is worthy of note.

Another strength of the study was the articulation of key factors which were presumed to affect the effectiveness of the intervention. This was done right at the beginning of the study in order to identify possible solutions to address the possible influence of these factors either during the intervention itself or during data analyses. These effect moderators included individual level as well as organisational and system-wide factors which are documented in the literature or have been observed in the study setting. These factors were further explored during the qualitative phase to provide context for the intervention, thereby adding credibility to the interpretation of the quantitative findings.

The study also used one of the highly recognised impact evaluation designs to assess the sustainability of the study intervention. Traditional implementation research involves testing the effectiveness of an intervention following its introduction but without due regard to the sustainability once it has been discontinued. This part of the study was therefore a novel approach in the area of SAM which can be explored further in future research using other performance indicators of choice.

10.4. General study limitations

Despite all the measures taken to improve the design of the study intervention, there were some persistent facility-specific and system-wide challenges which hampered the implementation fidelity, particularly the implementation of the WHO guidelines. The effectiveness of this guideline-based intervention in improving treatment outcomes in the context of HIV infection can therefore not be precisely judged given this shortcoming. However, the researcher argues that this study suffered, to a

certain degree, an implementation failure rather than a theory/design failure. That is, the study involved a well-conceived intervention design which, unfortunately, was not *fully* implemented as intended due to some structural factors beyond the control of the researcher himself. For example, while all efforts were made to insure that nutritional therapy was consistent with the guidelines throughout the study period, this was sometimes hindered by occasional shortages of ingredients to prepared feeds. Similarly, as mentioned earlier, feeding was sometimes done by nurses who were undergoing rotation in the paediatric ward but had not been trained on how to prepared and administer feeds to SAM cases. This was the case when senior nurses who were more conversant with the guidelines were not available, particularly at night, to provide guidance to the inexperienced nurses. There little doubt that the inconsistencies in the quality of care over time may have led to concomitant changes in treatment outcomes.

Therefore, the researcher maintains the view that the findings about treatment outcomes in light of the study intervention should be considered conservatively. The lessons learnt from this study about the factors which hampered the implementation of the intervention as intended can be used in future to reinforce this intervention design. However, the intervention should be conducted in randomised and controlled conditions in order to enhance the validity of the findings.

10.5. Agenda for future research

Within the context of increased ART and PMTCT coverage in South Africa, there seems to be hope that the impact of HIV infection on SAM-CFRs may be reduced.

However, given the limited evidence on the most effective ways of managing SAM cases who are HIV infected, these group of patients will continue to pose some challenges to the health care workforce (Trahan et al. 2012). In light of the existing evidence, including the findings of the current study, the following questions, though not exhaustive, need further or new investigations using rigorous study designs in order to inform practice.

1. What is the most effective way to test for and treat TB SAM coinfection in resource-poor settings?
2. What is the optimal timing, regiment and dosing of ART for SAM cases who are HIV infected?
3. What are the most effective feeding and rehydration regimens for SAM cases with or without HIV infection that have severe diarrhoea?
4. What is the optimal choice of therapeutic feeds during the transition phase for HIV infected SAM cases
5. How long does it take SAM cases with or without HIV infection to achieve specific targets for nutritional recovery in terms of the weight for height Z-scores?
6. What are the independent and combined effects of nutritional rehabilitation and ART on immune reconstitution among children infected with HIV?
7. What are the pharmacokinetic implications of combined ART and broad-based antibiotics among SAM children who are HIV infected and have other co-morbid infections?

REFERENCES

A&D, 2011. Precision weighing balances. http://baby.balances.com/

Ahmed T., Ali M., Ullah M., Choudhury I., Haque M., Salam M., Rabbani G., Suskind R., Fuchs G. 1999. "Mortality in severely malnourished children with diarrhoea and use of a standardised management protocol". *The Lancet* 353: 1919-1922.

Ahmed, T., Ali, M., Ullah, M. M., et al. 1999. "Mortality in severely malnourished children with diarrhoea and use of a standardised management protocol". *Lancet.* 353(9168):1919–22.

Amadi, B et al. 2001. "Intestinal and sytemic infection, HIV and mortality in Zambian children with persistent diarrhea and malnutrition". *Journal of Paediatric Gastroenterology and Nutrition.* 325:550–4.

Andersen, S. 1964. "Operations Research in Public Health". *Public Health Reports.* 79(4): 297–306.

Ashworth, A., Chopra, M., McCoy, D., et al. 2004. "WHO guidelines for management of severe malnutrition in rural South African hospitals: effect on case fatality and the influence of operational factors". *The Lancet.* 363(9415):1110–5.

Ashworth, A., Khanum, S., Jackson, A., and Schofield C. 2003. "Guidelines for the inpatient treatment of severely malnourished children. New Delhi: World Health Organization Regional Office for South-East Asia. pp. 5– 6.

Ashworth, A., Puoane, T., Schofield, C., and Sanders, D. 2003. "Improving the management of severe malnutrition. A guide for trainers. http://www.foodsecuritynetwork.org/resources/food_security/health/improving_the_management_of_severe_malnutrition.pdf. (Accessed 08 September 2012).

Ayieko, P., Ntoburi, S., Wagai, J., Opondo, C., Opiyo, N., et al. 2011 "A Multifaceted Intervention to Implement Guidelines and Improve Admission Paediatric Care in Kenyan District Hospitals: A Cluster Randomised Trial". *PLoS Medicine* 8(4): e1001018. doi:10.1371/journal.pmed.1001018

Bachou, H., Tylleskar, T., Downin,g R., et al. 2006. "Severe malnutrition with and without HIV-1 infection in hospitalized children in Kampala, Uganda : Differences in clinical features, haematological findings and CD4+ cell count". *Nutrition Journal.* 5:27.

Bailey, N. T. J. 1957. "Operational research in hospital planning and design". *Operational Research Quarterly.* 8 (3):149

Bairagi, R. 1981. "On validity of some anthropometric indicators as predictors of mortality". *American Journal of Clinical Nutrition.* 34:2592–4.

Baum, F. 1999. *The new Public Health: An Australian perspective.* London: Oxford Press.

Biglan, A., Metzler, C. W., and ALy, D. V. (1994). "Increasing the prevalence of successful children: The case for community intervention research". *Behaviour Analyst.* 17,335-351.

Black, R. et al. 2013. "Maternal and child undernutrition and overweight in low-income and middle-income countries". *Lancet,* 382:427–51.

Blake, R. 1989. "Integrating Quantitative and Qualitative Methods in Family Research". *Families Systems and Health.* 7:411–427.

Bower, M., et al. 2005. "Immune Reconstitution Inflammatory Syndrome Associated With Kaposi's Sarcoma'. *JCO* 23 (22) 5224-5228.

Briend, A., Garenne, M., Maire, B., et al. 1989. "Nutritional status, age and survival: the muscle mass hypothesis". *European Journal of Clinical Nutrition.* 43(10):715–26.

Bryman, A., and Burgess, R. 1994. Qualitative Data Analysis for Applied Policy Research: In Analyzing Qualitative Data: Routledge, New York 1994: Pg 164-180.

Burgess, RG. 1991. "Keeping field notes" (pp. 191-194). In RG Burgess (Ed.) Field Research: A sourcebook and Field Manual. London: Routledge.

Cavalcante, A. A., Pinheiro, L. M., Monte, C., et al. 1998. "Treatment of malnutrition in Brazil: simple solutions to common problems". *Tropical Doctor.* 28(2):95–7.

Cavalcante, A.A.M.; Pinheiro, L.M.P.; Monte C; Guimaraes, A.R.P., Ashworth, A. 1998. "Treatment of malnutrition in Brazil: simple solutions to common problems". *Tropical Doctor.* 28: 95-97.

Chen, H.-T. & Rossi, P. 1987. "The theory-driven approach to validity". *Evaluation and Program Planning,* 10, 95-103.

Chen, H.T. 1990. *Theory-driven evaluations,* Newbury Park, California, Sage Publications.

Chester, T. E. 2007. "The Guillebaud Report: Committee of enquiry into the Cost of the National Health Service". *Public Administration*. 34(2): 199-210.

Chima, C. S., Barco, K., Dewitt, M. L. A, Maeda, M., Teran, C., and Mullen KV. 1997. "Relationship of nutritional status to length of stay, hospital Hospital costs, and discharge status of patients hospitalised in the medicine service". *Journal of the American dietetic association*. 99:975-978.

Chinkhumba, J., Tomkins, A., Banda, T., et al. 2008. "The impact of HIV on mortality during inpatient rehabilitation of severely malnourished children in Malawi". *Transactions of the Royal Society of Tropical Medicine and* Hygiene. 102:639-44.

Churchman, C. W., Ackoff, R. L., and Arnoff, E. L. 1957. *Introduction to operations research*. John Wiley & Sons, Inc., New York.

Clute, K.F. 1963. *The General Practitioner: A Study of Medical Education and Practice in Ontario and Nova Scotia*. Toronto: University of Toronto Press, chapters 1, 2, 16, 17 and 18.

Collin, S. 2007. "Treating severe acute malnutrition seriously". *Archives of Disease in Childhood*.92:453–461. doi: 10.1136/adc.2006.098327.

Collins, S., Dent, N., Binns, P., Bahwere, p., Sadler, K., and Hallam, A. 2006. "Management of severe malnutrition in children". *The Lancet*. 368: 1992–2000.

Committee of Enquiry. 1958. Symposium on Operational Research in the National Health Service. J R Soc Med: 51: 139-145,

Cook, R. 1971. "Is hospital Hospital the place for the treatment of malnourished children"? *Journal of Tropical Paediatrics and Environmental Child Health*. 17: 15–25.

Cook, R. 1971. "Is hospital Hospital the place for the treatment of malnourished children"? *Journal of Tropical Paediatrics*. 17: 15–25.

Cook, T.D., and Campbell, D.T. 1979. Quasi-experimentation. Design & analysis issues for field settings. Boston, MA: Houghton Mifflin Company.

Creswell, j. w, and Clark V L. 2011. *Designing and Conducting Mixed Methods Research*. 2nd edition. SAGE publications, Inc.
http://www.sagepub.com/upm-data/35003_Chapter1.pdf
(accessed 22 January 2013).

Creswell, J.W., and Clark, V.L. 2007. *Designing and Conducting Mixed Methods Research*. Thousand Oaks, CA: Sage Publications.

Cuming K., Puoane T., Sanders D., Ashworth A. 2007. "Improving the quality of care of severely malnourished children: why do some rural hospitals perform consistently better than others"? *Health Policy and Planning. 1-10.*

Daly, J., McDonald, I., Willis, E.1992. Why don't you ask them? A qualitative Research Framework for investigating the Diagnosis of Cardiac Normality. In: Daly J,McDonald I, Willis E, eds. *Researching Health Care: Designs, Dilemmas, and Disciplines*. London: Routledge, 1992:189-206.

De Maayer, T., and Saloojee, H. 2011. "Clinical outcomes of severe malnutrition in a high tuberculosis and HIV setting". *Arch Dis Child* 96(6): 560-4.

Deen, J. L., Funk, M., Guevara, V. C, Saloojee, H., Doe, J. Y., Palmer, A., et al. 2003. "Implementation of WHO guidelines on management of severe malnutrition in hospitals in Africa. *Bulletin of the World Health Organization* 81: 237-43.

Deen, J. L., Funk, M., Guevara, V. C., et al. 2003. "Implementation of WHO guidelines on management of severe malnutrition in hospitals in Africa". *Bulletin of the World Health Organisation*. 81(4):237–43.

Donabedian, A. 2005. "Evaluating the quality of medical care". *The Milbank Quarterly*, 83(4): 691–729.

Donabedian, A. 1988. "The quality of care: How can it be assessed"? *Journal of American Medical Association*. 260(12):1743-1748.

Emerson, M. E. 1995. Writing ethnographic field notes. University of Chicago Press.

European Consultants Organisation. 2005. The district profile of the Eastern Cape O.R. Tambo District Municipality. http://www.ewisa.co.za/eWISAWaterworks/misc/MunicipalDocuments/ECDisO.R_ Tambo/290806175904.pdf (Accessed 15 April 2013).

Fergusson, P., and Tomkins, A. 2009. "HIV prevalence and mortality among children undergoing treatment for severe acute malnutrition in Sub-Saharan Africa: a systematic review and meta-analysis". *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 103:541–8.

Garrow, J. S., Picou, D., and Waterlow, J. C. (1962). "The treatment and prognosis of infantile malnutrition in Jamaican children". *West Indies Medical Journal*. 11: 217– 227.

Garrow, J. S., Smith, R., and Ward, E. E. 1968. Electrolyte metabolism in severe infantile malnutrition. Oxford: Pergamom Press.

Gillings, D., Makuc, D., and Siegel, E. 1981. "Analysis of interrupted time series mortality trends: an example to evaluate regionalized perinatal care". *American Journal of Public Health*. 71, 38–46.

Glouberman, S. and Zimmerman, B. 2002. Complicated and complex systems: what would successful reform of Medicare look like? Commission on the Future of Health Care in Canada. Canada.

Golden, M. H. N. (1998). Oedematous malnutrition. British Medical Bulletin.2:433-444

Gomez, F., Ramos, G. R., Frenk, S., Cravioto, M. J., Chavez, R., and Vazquez, J. 2000. "Mortality in second and third degree malnutrition". *Bulletin of the World Health Organisation*. 78(10):1275-1280.

Gould, J. B. 2006. "Operational research on perinatal epidemiology, care and outcomes". *Journal of perinatology*. 265:34-37.

Greene, J. C., Caracelli, V. J., and Graham, W. F. 1989. "Toward a conceptual framework for mixed-method evaluation designs". *Educational Evaluation and Policy Analysis. 11*(3):255–274.

Grellety, Y. 2000. The management of severe malnutrition in Africa (dissertation). University of Aberdeen. http://files.ennonline.net/attachments/1016/yg-thesis.pdf (Accessed 22 December 2013).

Hay, R. W., and Whitehead, R. G. 1973. The therapy of the severely malnourished child: A practical manual. Makerere (Uganda): National Food and Nutrition Council of Uganda in collaboration with the MRC Child Nutrition Unit.

Heikens, G. T. 2007. "How can we improve the care of severely malnourished children in Africa": *PLoS Medicine*.4:2.

Hendrickse RG (1991). Protein-energy malnutrition. In: Hendrickse RG, eds Paediatrics in the Tropics. London: Blackwell Scientific Publication: 119-131.

Hines, F. 2013. *Determining Focus Group Specifications: How to Make the Difficult Trade-offs. Research, strategy and innovation*. Hines & Lee, Inc. http://www.hinesandlee.com/sites/default/files/Hines%2BLee-FocusGroupSpecifications.pdf (Accessed 23 January 2013).

Ivankova, V. N., Creswell, J. W., Stick, S. L. 2006. "Using Mixed-Methods Sequential Explanatory Design: From Theory to Practice". *Field Methods* 18: 3.

Jackson A., Ashworth A., Khanum S. 2006. "Improving child survival: Malnutrition Task Force and the paediatrician's responsibility". *Archives of Disease I n Childhood* 91: 706-710.

Jelliffe, D. J. 1970. " The children's ward as lethal factor". *Journal of Paediatrics*. 77: 895- 899.

Jensen, G. L., Mirtallo, J., Compher, C., et al. 2010. "Adult starvation and disease-related malnutrition: A proposal for aetiology-based diagnosis in the clinical practice setting from the International Consensus Guideline Committee". *Journal of Parenteral and Enteral Nutrition*. 34(2):156-159.

Joosten, K. F., and Hulst, J. M. 2008. "Prevalence of malnutrition in paediatric hospital Hospital patients". *Current Opinion in Paediatrics*. 20(5):590-596.

Kamangar, F. 2012. "Effect modification in epidemiology and medicine". *Archive of Iranian Med*. 15(9):575-82. doi: 012159/AIM.0014.

Karaolis N., Jackson D., Ashworth A., Sanders D., Nonzwakazi S., McCoy D., Chopra M., Schofield C. 2007. "WHO guidelines for severe malnutrition: are they feasible in rural African hospitals"? *Archives of Disease in Childhood*. 92: 198-204.

Kessler, L., Daley, H., Malenga, G., et al. 2000. "The impact of the Human Immunodeficiency Virus type 1 on the management of severe malnutrition in Malawi". *Annal of Tropical Paediatrics*. 201:50-6.

Kilpatrick, G.S. January, 1963. Observer error in medicine. *Journal of Medical Education* 38:38–43

Kitinger, J. 1995. "Qualitative Research: introducing focus groups". *The British Medical Journal. 311*(700): 299-302.

Koethe, J. R., Heimburger, D. C. 2010. "Nutritional aspects of HIV-associated wasting in sub-Saharan Africa". *American Journal of Clinical Nutrition*. 91:1138S–1142S.

Krueger, R. 1994. *Focus Groups: A Practical Guide for Applied Research.* Thousand Oaks: Sage Publications.

Latham, MC. 1991. "The dermatosis of kwashiorkor in young children". *Semin Dermatol.* 10(4):270-2.

Liefooghe, R., Michiels, N., Habib, S., Moran, M., and De Muynck, A. 1995. "Perception and Social consequences of Tuberculosis: A focus group study of Tuberculosis patients in Sialkot, Pakistan". *Social Science Medicine* 41(12): 1685-1692.

McCann, M. 2007. *Programme of Support to Local Economic Development in the Eastern Cape. Competitive Advantage Assessment and Training Support Project.* European Consultants Organisation. http://www.ewisa.co.za/ewisawaterworks/misc/MunicipalDocuments/ECDisO.R_T ambo/290806175904.pdf (Accessed 21 March 2013)

Madec, Y. et al. 2011. "HIV prevalence and impact on renutrition in children hospitalised for severe malnutrition in Niger: an argument for more systematic screening". *Plos one.* 6(7): e22787. doi:10.1371/journal.pone.0022787

Maitland, K., Berkley, J. A., Shebbe, M., Peshu, N., English, M., et al. 2006. "Children with severe malnutrition: Can those at highest risk of death be identified with the WHO protocol"? *PLoS Med.* 3(12): e500. doi:10.1371/journal.pmed. 0030500.

Marchal, B., Van Belle, S., Kegels, G., et al. 2010. Theory driven inquiry for health systems research. Institute of tropical Medicine, Health Care Management Unit, Department of Public Health. Antwerp. http://www.itg.be/internet/ds/tde/tde.html (Accessed 23 May 2014).

Marshall, C., and Rossman, G. 1999. *Designing Qualitative Research.* 3rd Ed. London: Sage publications.

Mehta, N. M., et al. 2013. "Defining Paediatric Malnutrition: A Paradigm Shift toward Aetiology-Related Definitions". *Journal of Parenteral and Enteral Nutrition. 37(4): 460-81.*

Messner, R. L., Stephens, N., Wheeler, W. E., Hawes, M. C., 1991. "Effects of admission nutritional status on length of hospital stay". *Gastro-enterology and Nursing* . 2002- 2005.

Mgone, C. S., Mhalu, F. S., Shao, J. F., et al. 1991. "Prevalence of HIV-1 infection and symptomatology of AIDS in severely malnourished children in Dar Es Salaam, Tanzania". *Journal of Acquired Immune Deficiency Syndrome.* 4: 910-13.

Miles, M., and Huberman, A. 1999. *Qualitative Data Analysis*: London: Sage. Pg 22-24.

Morgan, D L. 1998. Planning Focus Groups. SAGE Publications, p. 61.

Morse, J. M. 1991. "Approaches to qualitative-quantitative methodological triangulation". *Nursing Research.* 40:120–23.

Municipal Demarcation Board. 2008. *Assessment of capacity for the 2008/09 period. District municipality report. OR Tambo district municipality (D15).* Eastern Cape. http://www.demarcation.org.za/index.php/downloads/documents/circulars (Accessed 15 April 2013).

Ndekha, M. J., Mnary, M. J., Ashorn, P. Et al. 2004. "Home based therapy with ready to use therapeutic food is of benefit to malnourished, HIV-infected Malawian children". *Journal of Paediatric Gastroenterology and Nutrition.* 942:222-5

Pelletier, D. L., Frongillo, E. A., Schroeder, D. G., Habicht, J.P. 1995. "The effects of malnutrition on child mortality in developing countries". *Bulletin of the World Health Organisation.* 73(4):443-448.

Penfold, R. B., Zhang, F. 2013. Use of interrupted time series analysis in evaluating health care quality improvements. Academic Pediatrics 2013, 13:S38–S44.

Picou, D., Alleyne, G. A. O., Brooke, O., Kerr, D. S., Miller, C., et al. 1978. "Malnutrition and gastroenteritis in children: A manual for hospital treatment and management". Kingston: Tropical Metabolism Research Unit.

Pope, C., and Mays, N. 1995. "Qualitative Research: Researching the parts other methods cannot reach: An introduction to Qualitative methods in health and health services research". *British Medical Journal,* 311(6996):42-45.

Pope, C., Ziebland, S., Mays, N. 2000. "Qualitative Research in Health Care: Analyzing Qualitative Data". *British Medical Journal.* **320**: 114-116.

Prazuck, T., Tall, F., Nacro, B., t al. 1993. "HIV infection and severe malnutrition: a clinical and epidemiological study in Burkina Faso". *AIDS;* 7: 103–08.

Prendergast, A., Dangarembizi, B. M., Kitaka, B. S., Natukunda, E., et al. 2011. "Hospitalisation for severe malnutrition among HIV infected children starting antiretroviral therapy". *AIDS*. 25: 951 – 956.

Pretorius, P.J., Hansen, J.D., Davel, J. G. A., and Brock, J. F, 1956. "Skimmed milk and kwashiorkor". *South African Medical Journal*. 33: 447–450.

Prudhon, C., Briend, A., Laurie,r D., Golden, M. H., and Mary, J. Y. 1996. "Comparison of weight- and height-based indices for assessing the risk of death in severely malnourished children". *American Journal of Epidemiology*. 144: 116–23.

Puoane et al. 2006. "Training nurses to save lives of malnourished children". *Curationis*. 29 (1): 73-78.

Puoane, T., Sanders, D., Ashworth, A., Chopra, m., Strasser, S., and McCoy, D. 2004. "Improving the hospital management of malnourished children by participatory research" *International Journal for Quality in Health Care*. 16:31- 40.

Puoane, T., Sanders, D., Ashworth, A., and Ngumbela M. 2006. "Training nurses to save lives of malnourished Children". *Curationis*, Vol 29(1): 73-78.

Puoane, T., Cuming, K., Sanders, D., Ashworth, A. (2008). Why do some hospitals achieve better care of severely malnourished children than others? Five-year follow-up of rural hospitals in Eastern Cape, South Africa. *Health Policy and Planning*.1–10

Ramsay, C. R., Matowe, L., Grilli, R., Grimshaw, J. M., Thomas, R. E. 2003. "Interrupted time series designs in health technology assessment: Lessons from two systematic reviews of behavior change strategies". *Int.J.Technol.Assess.Health Care*. 19:613-23.

Ringner, M. 2008. "What is principal component analysis"? *Nature Biotechnology*. **26**, 303 - 304 doi:10.1038/nbt0308-303.

Robinson, G., Goldstein, M., Levine, G. M. 1987. "Impact of nutritional status on DRG length of stay". *Journal of Parenteral and Enteral Nutrition*: 11: 49-51.

Rossi. P.H., Lipsey, M.W, & Freeman, H.E. (2004). *Evaluation. A systematic approach* (7th edition) Thousand Oaks: Sage Publications.

Rossman, G., and Wilson, B. 1991. Numbers and Words Revisited: Being "Shamelessly Eclectic." *Evaluation Review*. 9(5):627–643.

Sandelowski, M. 2000. "Whatever happened to Qualitative description"? *Research in Nursing and Health.* 23.334-340.

Sandige, H., Ndekha, M. J., Briend, A., et al. 2004. "Home-based treatment of malnourished Malawian children with locally produced or imported ready-to-use food". *Journal of Paediatric Gastroenterology and Nutrition.* 392:141–6.

Savadogo, G. L., Donnen, P., Koueta, F., Kafando, F., Hennart, P., and Dramaix, M. 2013. "Impact of HIV/AIDS on mortality and nutritional recovery among hospitalised severely malnourished children before starting antiretroviral treatment". *Open Journal of Paediatrics.* 3: 340-345.

Schofield, C., and Ashworth, A. 1996. "Why have mortality rates for severe malnutrition remained so high"? *Bulleting of the World Health Organisation.* 74: 223–29.

Schofield, C., and Ashworth, A. 1997. "Severe malnutrition in children: high case-fatality rates can be reduced". *Africa Health,* September issue, 17- 18.

Schub, C. 2010. "Management of severe malnutrition". *South African Journal of Clinical Nutrition.* 23(1).

Serumaga, B., Ross-Degnan, D., Avery, A. J., Elliott, R. A., Majumdar, S. R., Zhang, F., Soumerai, S. B. 2011. Effect of pay for performance on the management and outcomes of hypertension in the United Kingdom: interrupted time series study. BMJ. 2011, 342:d108.

Shadish, R.W., Cook, D.T., and Campbell D.T. 2002. *Experimental and Quasi-Experimental Designs for Generalized Causal Inference.* Houghton Mifflin Company, Boston. USA.

StataCorp. 2013. *Stata Statistical Software: Release 13.* College Station, TX: StataCorp LP.

Taljaard, M. et al. 2014. "The use of segmented regression in analysing interrupted time series studies: an example in pre-Hospital ambulance care". Implementation Science 9 (77)

Tashakkori, A., and C. Teddlie. 1998. "Mixed methodology: Combining qualitative and quantitative approaches". *Applied Social Research Methods Series,* vol. 46. Thousand Oaks, CA: Sage.

Thadhani, R., and Tonelli, M. 2006. "Cohort Studies. Marching forward". *Clinical Journal of the American Society of Nephrology.* 1: 1117–1123, 2006. doi: 10.2215/CJN.00080106.

Thiry, K., Hassey, A., and Sullivan, F. 2003. "Systematic review of scope and quality of electronic patient record data in primary care". *BMJ 2003;326:1070.*

Ticklay, I. M., Nathoo, K. J., Siziya, S., and Brady, J. P. 1997. "HIV infection in malnourished children in Harare, Zimbabwe". *East African Medical* Journal. 74: 217– 20.

Trehan, I., O'Hare, A., Phiri, A., Heikens, G. T. 2012. Challenges in the management of HIV – infected malnourished children in Sub-Saharan Africa. *AIDS Research and Treatment.* 10: 8-16.

UN. 2007. Community-based management of severe acute malnutrition. A joint statement by the World Health Organization, World Food Programme, United Nations Standing Committee on Nutrition, United Nations Children's Fund. Geneva: World Health Organization/World Food Programme/United Nations Standing Committee on Nutrition/United Nations Children's Fund. http://www.who.int/nutrition/topics/Statement_community_based_man_sev_acu te_mal_eng.pdf?ua=1 (Accessed 15 April 2013).

UNHCR. 1999. *Handbook for emergencies,* 2nd edition. Geneva: UNHCR. http://www.the- ecentre.net/resources/e_library/doc/han_Em.pdf (Accessed 10 December 2013).

UNICEF. 2009. Tracking Progress on Child and Maternal Nutrition. http://www.unicef.org/publications/index.html. (Accessed 10 December 2013).

UNICEF. 2012. Nutrition in Emergencies: the Harmonised training package: Resource Material for Training on Nutrition in Emergencies. UNICEF. http://www.unicef.org/nutrition/training/2.4/1.html (Accessed 16 April 2013).

UNICEF. 2013. Global child malnutrition trends (1999 – 2012). UNICEF, New York. http://www.childinfo.org/malnutrition_dashboard.html (Accessed 9 January 2014).

United Nations Interagency Group for Child Mortality Estimation. 2012. *Levels and trends in child mortality*. Report 2012. New York, United Nations Children's Fund.

Von Elm, E., Altman, G. d., Egger, M., Pocock, S. J., Gøtzsche, C. P., and Vandenbroucke, J. P. 2007. "The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies". *Bulletin of the World Health Organisation*. 85(11): 867-872.

Von Elm, E., Altman, G. d., Egger, M., Pocock, S. J., Gøtzsche, C. P., and Vandenbroucke, J. P. 2008. "The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies". *Journal of Clinical Epidemiology*. 61(4):344-9. PMID: 18313558.

Wagner, A.K., Soumerai, S. B., Zhang, F., and Ross-Degnan D. 2002. "Segmented regression analysis of interrupted time series in medication use research". *Journal of Clinical Pharmacy and Therapeutics*: 27, 299–309".

Waterlow, J. C. 1986. "Metabolic adaptation to low intakes of energy and protein". *Annual Review of Nutrition*. 6: 495–526.

Waterlow, J. 2006. *Protein energy-malnutrition*. Reprint with supplementary material Herts: Smith-Gordon.

WHO. 1981. *The treatment and management of severe protein energy malnutrition*. Geneva: WHO.

WHO. 1999. Management of severe malnutrition: a manual for physicians and other senior health workers. Geneva. http://whqlibdoc.who.int/hq/1999/a57361.pdf (Accessed 12 January 2012).

WHO. 2000. *Management of the child with a serious infection or severe malnutrition: guidelines for care at the first-referral level in developing countries*. Geneva: WHO. http://whqlibdoc.who.int/hq/2000/WHO_FCH_CAH_00.1.pdf. (Accessed 10 December 2013).

WHO. 2002. Training course on the management of severe malnutrition: Principles of care. Department of nutrition for health and development. Geneva. http://www.who.int/nutrition/publications/en/manage_severe_malnutrition_training_fly_eng.pdf. (Accessed 16 April 2013).

WHO. 2004. Severe malnutrition: Report of a consultation to review current literature 6-7 September 2004. World Health Organisation, Geneva. http://www.who.int/nutrition/publications/severemalnutrition/9241593318_repo rt.pdf?ua=1 (Accessed 30 June 2014).

WHO. 2005. *Interim WHO clinical staging of HIV/AIDS and HIV/AIDS case definitions for surveillance (African Region)*. World Health Organization http://www.who.int/hiv/pub/guidelines/casedefinitions/en/index.html. (Accessed 20/07/2012).

WHO. 2006. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards based on length/height, weight and age. *Acta Paediatrica Supplement*. 450:76-85.

WHO. 2007. Joint United Nations Programme on HIV/AIDS. AIDS epidemic update. Geneva. Switzerland. http://www.who.int/hiv/pub/epidemiology/epiupdate2007/en/ (Accessed 20 December 2013).

WHO. 2008. *Framework for Operations and Implementation Research in Health and Disease Control Programs*. Geneva, Switzerland. http://whqlibdoc.who.int/publications/2008/9292241109_eng.pdf?ua=1 (accessed 21 January 2013).

WHO. 2009. *WHO child growth standards and the identification of severe acute malnutrition in infants and children. A joint statement by the World Health Organization and the United Nations Children's Fund*. Geneva: World Health Organization. http://apps.who.int/iris/bitstream/10665/44129/1/9789241598163_eng.pdf (Accessed 10 December 2013).

WHO. 2010. Improving the Inpatient Management of Severe Acute Malnutrition: Toolkit to monitor current management of severe acute malnutrition. http://www.cmamforum.org/Pool/Resources/Toolkit-to-monitor-management- SAM-2010.pdf (Accessed 12 January 2012).

WHO. 2013. Guideline: updates on the management of severe acute malnutrition in infants and children. WHO Library Cataloguing-in-Publication Data. World Health Organization; ISBN 978 92 4 150632 8

WHO. 2014. Summary of the key facts about the 2012 joint malnutrition estimates. WHO Geneva. http://www.who.int/nutgrowthdb/estimates2012/en/ (Accessed 9 January 2014).

WHO/UNICEF. 2009. A Joint Statement by the World Health Organization and United Nations Children's Fund. *WHO child growth standards and the identification of severe acute malnutrition in infants and children.* WHO/UNICEF. Geneva. Switzerland.

Wilkinson, D., Scrace, M., and Boyd, N. 1996. "Reduction in in-hospital Hospital mortality of children with malnutrition". *Journal of Tropical Paediatrics*, 42: 114-115.

Wilkinson, D., Scrace, M., and Boyd, N. 1996. "Reduction in in-hospital Hospital mortality of children with malnutrition". *Journal of Tropical Paediatrics*. 42: 114-115.

LIST OF APPENDICES

Appendix 1: Consent forms for mothers – Xhosa

UNIVERSITY OF THE WESTERN CAPE

School of Public Health

Private Bag X 17, Bellville 7535, South Africa

Tel: +27 21-9592809, Fax: 27 21-9592872

A WHO Collaborating Centre for Research and Training in Human Resources for Health Development

IFOMU YOVUMELWANO

Uhlolo lokuzalisekisa kwemigaqo ka-WHO engqamene nokungondleki ngenxa yolwazi nge-HIV/AIDS eMpuma Kapa

Olu phando luchazwe ngolwimi endilwaziyo kwaye ndiyavuma ukuthatha inxaxheba kuba ndithanda. Imibuzo yam ngokungqamene nophando iphendulwe. Ndiyaqonda ukuba iinkcukacha ngesazisi sam aziyi kupapashwa kwaye ndingayirhoxisa inxaxheba yam ngaphandle kwesizathu ngaliphi na ixesha kwaye andiyi kuchapazeleka kakubi.

Igama lomthathi-nxaxheba

Utyikityo lomthathi-nxaxheba

Ingqina

Umhla

Ukuba unayo nayiphi na imibuzo malunga noluphando okanye ufuna ukuxela iingxaki obe nazo ngokungqamene nophando, nceda uqhagamshele nomququzeleli wophando:

Igama lomququzeleli wophando: Moise Muzigaba

University of the Western Cape

Private Bag X17, Belville 7535

Telephone: (021)959- 9392

Cell: 0730651833

Email: mochemoseo@yahoo.co.uk

Appendix 2: Consent forms for mothers – English

UNIVERSITY OF THE WESTERN CAPE

School of Public Health

Private Bag X 17, Bellville 7535, South Africa

Tel: +27 21-9592809, Fax: 27 21-9592872

A WHO Collaborating Centre for Research and Training in Human Resources for Health Development

CONSENT FORM FOR THE MOTHER

The WHO 10-step treatment modality for severe malnutrition in the context of HIV/AIDS comorbidity: An operational research in the Eastern Cape Province

The study has been described to me in a language that I understand and I freely and voluntarily agree to participate. My questions about the study have been answered. I understand that my identity will not be disclosed and that I may withdraw from the study without giving a reason at any time and this will not negatively affect me in any way.

Participant's name.....

Participant's signature.....

Witness.....

Date.....

Should you have any questions regarding this study or wish to report any problems you have experienced related to the study, please contact the study coordinator:

Study Coordinator's Name: Moise Muzigaba

University of the Western Cape

Private Bag X17, Belville 7535

Telephone: (021)959- 9392

Cell: 0730651833

Email: mochemoseo@yahoo.co.uk

Appendix 3: Participant information sheet for mothers- English

UNIVERSITY OF THE WESTERN CAPE

School of Public Health

Private Bag X 17, Bellville 7535, South Africa

Tel: +27 21-9592809, Fax: 27 21-9592872

A WHO Collaborating Centre for Research and Training in Human Resources for Health Development

INFORMATION SHEET FOR THE MOTHER

The WHO 10-step treatment modality for severe malnutrition in the context of HIV/AIDS comorbidity: An operational research in the Eastern Cape Province

What is this study about?

This is a research project being conducted by a PhD student and Professors from the School of Public Health at the University of the Western Cape. We are inviting you to participate in this research project because your child has been admitted to this hospital Hospital with severe malnutrition which is the problem that this research seeks to investigate. We are conducting a research on issues related to the hospital Hospital management of severely malnourished children, a condition that affects many young children in South Africa, especially in the Eastern Cape Province. The majority of children who are admitted to hospitals recover very slowly. In order to find ways to speed the recovery of malnourished children and reduce the length of hospital Hospital stay, we need a better understanding of what problems are contributing factors towards poor recovery of these children, by making sure that hospital Hospital staff members are familiar with modern, effective guidelines for the management of severe malnutrition and use them. These guidelines include giving correct amounts of fluids, feeding correctly, treating infections and also correcting electrolyte and macronutrient deficiencies in patients. Information collected in this research will assist health professions to plan strategies to improve the management of severe malnourished children in hospitals.

What will I be asked to do if I agree to participate?

You will be asked sign a consent form to allow us to conduct screening for your child's HIV status and monitor your child during treatment which will be done using treatment methods recommended by experts in the field. Trained researchers will also make observations of all activities involved in the management of severe malnourished patients to ensure that they are implemented optimally Screening will be done by trained hospital Hospital nursing sisters, which will draw a small sample of blood (equivalent to one

teaspoon) to be analysed by a qualified laboratory technician. Counselling services will be offered to you before and after your child has been tested for HIV.

Would my participation in this study be kept confidential?

We will do our best to keep your personal information confidential. To help protect your confidentiality, only the researchers will have access to the information collected about your child and yourself. Your child's name will not be used; only numbers will be used as a form of identification. Once the research is completed, the data will be locked up at the University of the Western Cape. If we write a report or article about this research project, your identity will be protected to the maximum extent possible. In accordance with legal requirements and/or professional standards, we will disclose to the appropriate individuals and/or authorities information that comes to our attention concerning child abuse or neglect or potential harm to you or others.

What are the risks of this research?

As the focus of this research is on children under the age of 5 years, all research procedures will be carried out in their best interest as required by Section 130 of the *Children's Act* (No. 30 of 2010), *The National Policy on HIV Counselling and Testing*, as well as the *Guidelines on Testing Children for HIV*.

The researcher acknowledges that, although not foreseeable in this research, participation in the human testing and counselling (HTC) may lead to some physical harm on the child, as well as impact the moral, emotional, and spiritual welfare of the child's family and loved ones. However, all the necessary measures will be put in place to ensure that all these harms are minimised. For example testing of HIV will be done by professional nurses who will adhere to the standard protocol for testing in order for example to minimise transmission of infection through needle pricks and other sharp materials. Pre- and post- counselling services will also be offered to parents/guardians whose children test positive for HIV infection.

What are the benefits of this research?

This research is not designed to help you personally, but the results may help the investigator learn more about on issues related to the hospital Hospital management of severely malnourished children, a condition that affects many young children in South Africa. We hope that, in the future, other people might benefit from this study through improved understanding of these issues. Once the project is completed however, you will be invited for the presentation of the results at a meeting in your local health facility/hospital.

Do I have to be in this research and may I stop participating at any time?

The participation of your child in this research is completely voluntary. You may choose not to let your child take part at all. If you decide that your child can participate in this research, you may stop his/her participating at any time without having to give a reason. If you decide not to let him/her participate in this, you or your child will not be penalized or lose

any benefits to which you otherwise qualify. The care of your child will not be influenced by your decision.

What if I have questions?

This research is being conducted by ***Moise Muzigaba from*** the University of the Western Cape. If you have any questions about the research study itself, please contact the following person:

Study Coordinator's Name: Moise Muzigaba

University of the Western Cape

Private Bag X17, Belville 7535

Telephone: (021)959- 9392

Cell: 0730651833

Email: mochemoseo@yahoo.co.uk

This research has been approved by the University of the Western Cape's Senate Research Committee and Ethics Committee.

Appendix 4: Participant information sheet for mothers- Xhosa

UNIVERSITY OF THE WESTERN CAPE

School of Public Health

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Tel: +27 21-9592809, Fax: 27 21-9592872

A WHO Collaborating Centre for Research and Training in Human Resources for Health Development

Isihloko somsebenzi: Uphando lokuzalisekisa kwemiqago ka-WHO yokungondleki ngenxa yolwazi ngokungqamene neHIV/AIDS eMpuma Kapa.

Imida yophando

Olu luphando olwenziwa ngumfundi wePhD kunye noojingalwazi weSikolo seMpilo kaWonke-wonke /soLuntu eYunivesithi yaseWestern Cape. Siyakumema ukuba uthathe inxaxheba kolu phando lolwazi kuba umntwana wakho ulaliswe kwesi sibhedlele engondlekanga, ingxaki leyo eya kuphandwa kolu phando.

Senza uphando ngemiba engqamene nolawulo lwabantwana abangondlekanga esibhedlele, imeko echaphazela abantwana abaninzi eMzantsi-Afrika, ingakumbi eMpuma Kapa. Uninzi lwabantwana abalaliswa esibhedlele bachacha kade. Ngenjongo yokufumana iindlela zokukhawulezisa uchacho lwabantwana abondlekanga nokucutha isithuba sokulaliswa esibhedlele, simele ukuba nolwazi ngeengxaki ezibangela ukuchacha kade ngokuqinisekisa ukuba abasebenzi esibhedlele banalo ulwazi ngemigaqo esebenzayo yale mihla. Le migaqo iquka ukunika imilinganganiselo efanelekileyo yezinto ezibumanzi, ukutyisa okufanelekileyo nokulungisa intswelo yezimbiwa nokutya okomeleza izigulana. Ulwazi oluvela kolu phando luya kunceda abo basebenza kwezempilo bacwangise iinkqubo zokuphucula ulawulo lwabantwana abangondlekanga ezibhedlele.

Ukuthatha inxaxheba kwam kuya kuquka ntoni?

Uya kucelwa ukuba utyikitye ifomu yovumelwano esinika thina imvume yokuqinisekisa imo yeHIV yomntwana wakho simjonge umntwana wakho ngesithuba sonyango oluya kwenziwa kusetyenziswa iindlela zokunyanga ezicetyiswe ziingcali zezempilo. Abaphandi abaqeqeshiweyo baya kuhlola yonke imisebenzi engqameme nolawulo lwezigulana ezingondlekanga ngenjongo yokuqinisekisa ukuba kusetyenzwe ngendlela efanelekileyo. Ukuqinisekisa imo yeHIV kuya kwenziwa ngabongikazi abaqeqeshelwe lo msebenzi, abaya kutsala intwana yegazi (elilingane netispuni) lihlolwe ngumsebenzi welebhu oqeqeshiweyo. Uya kunikwa ingcebiso phambi nangemva kokuqinisekisa imo yeHIV yomntwana wakho.

Ukuthatha inxaxheba kwam kuya kupapashwa?

Siya kuzama kangangoko sinako ukuzigcina iinkcukacha zakho kunye nezomntwana wakho zibe yimfihlo. Ngenjongo yokugcina imfihlo, ngabaphando bodwa abaya kuba nolwazi ngeenkcukacha zenu. Aliyi kusetyenziswa igama lomntwana wakho; kuya kusetyenziswa amanani njengezazisi kuphela. Lwakugqityezelwa uphando, ulwazi / iinkcukacha ziya kugcinwa eYunivesithi yaseWestern Cape. Ukuba kubhalwa ingxelo okanye umhlathi ngolu phando, isazisi sakho asiyi kupapashwa. Ngokweemfuno kwezomthetho nemigangatho yomsebenzi, siya kuxela nayiphi na impatho embi okanye umonakalo onokwenzeka kumntwana, kuwe okanye kwabanye, kubantu okanye iziphathamandla ezifanelekileyo.

Yintoni ingozi yolu phando?

Akukho ngozi iyaziwayo ingqamene nokumvumela umntwana wakho athathe inxaxheba kolu phando.

Yintoni inzuzo yolu phando?

Olu phando alujongani nokukunceda wena ngobuqu, kodwa iziphumo zinganako ukunceda umphandi abe nolwazi ngemiba engqamene nolawulo esibhedlele lwabantwana abondlekanga, imeko embi echaphazela abantwana abaninzi abancinane eMzantsi Afrika. Sinethemba lokuba kwixesha elizayo, abanye abantu bangaba nenzuzo ngenxa yolu phando ngokuba nolwazi olongezelelweyo ngokungqamene nale miba nokulungiswa kwayo. Wakugqityezelwa umsebenzi, uya kumenywa kupapasho lweziphumo entlanganisweni eya kuba kho kwiziko lezempilo lengingqi yakho /esibhedlele.

Ndimelwe ukuthatha inxaxheba kolu phando okanye ndingayeka nangaliphi na ixesha?

Nguwe onika imvume yokuba umntwana wakho angathatha inxaxheba kolu phando. Ungakhetha ukuba angathathi nxaxheba. Ukuba ugqiba ukuba umntwana angathatha inxaxheba,, ungayirhoxisa inxaxheba yakhe ngaliphi na ixesha ngaphandle kokunika isizathu. Ukuba ugqiba oku, wena nomntwana wakho aniyi kuchaphazeleka kakubi okanye nilahlekelwe yiyo nayiphi na inzuzo elungele nina. Ukukhathalela komntwana wakho akuyi kuchaphazeleka ngenxa yesigqibo sakho.

Imibuzo yam?

Olu phando lwenziwa ***nguMoise Muzigaba*** *weYunivesithi yaseWestern Cape. Ukuba unemibuzo ngokungqamene nophando olu, nceda uqhagamshele nalo mntu uchazwa ngezantsi:*

Igama lomququzeleli wophando:

Study Coordinator's Name: Moise Muzigaba

University of the Western Cape

Private Bag X17, Belville 7535

Telephone: (021)959- 9392

Cell: 0730651833

Email: mochemoseo@yahoo.co.uk

Olu phando luvunyelwe yiKomiti yoPhando neKomiti ejongene neNdlela yokuziPhatha yeYunivesithi yaseWestern Cape.

Appendix 5: Participant information sheet for hospital Hospital staff- English

UNIVERSITY OF THE WESTERN CAPE

School of Public Health

Private Bag X 17, Bellville 7535, South Africa

Tel: +27 21-9592809, Fax: 27 21-9592872

A WHO Collaborating Centre for Research and Training in Human Resources for Health Development

INFORMATION SHEET FOR THE HOSPITAL HOSPITAL STAFF

Project Title: The WHO 10-step treatment modality for severe malnutrition in the context of HIV/AIDS comorbidity: An operational research in the Eastern Cape Province

What is this study about?

This is a research project being conducted by a PhD student and Professors from the School of Public Health at the University of the Western Cape. We are inviting you to participate in this research project because your child has been admitted to this hospital Hospital with severe malnutrition, a problem that this research seeks to investigate.

We are conducting a research on issues related to the hospital Hospital management of severely malnourished children, a condition that affects many young children in South Africa, especially in the Eastern Cape Province. The majority of children who are admitted to hospitals recover very slowly. In order to find ways to speed the recovery of malnourished children and reduce the length of hospital Hospital stay, we need a better understanding of what problems are contributing factors towards poor recovery of these children, by making sure that hospital Hospital staff members are familiar with modern, effective guidelines for the management of severe malnutrition and use them. These

guidelines include giving correct amounts of fluids, feeding correctly, treating infections and also correcting electrolyte and macronutrient deficiencies in patients. Information collected in this research will assist health professions to plan strategies to improve the management of severe malnourished children in hospitals.

What will I be asked to do if I agree to participate?

Upon agreeing to participate in this project, you will be asked to participate in a group discussion with other health care givers from your hospital. This discussion will not take more than 1 hour of your time.

Would my participation in this study be kept confidential?

Your confidentiality may not be ensured during the discussion as what you share will be heard by people in the group. However, after the discussion, the researchers will play their part to ensure that information that you have shared is not revealed to any other person. All the recordings will be kept in a secure location and only accessible to personnel involved in the study. Maximum effort will be exercised to ensure that these details are only known to the researcher and the relevant health personnel in the hospital. After the data has been captured and backed up electronically, the recording containing your information will be erased.

What are the risks of this research?

There are no known risks associated with participating in this part of the study.

What are the benefits of this research?

This research is not designed to help you personally, but the results may help the investigator learn more about on issues related to the hospital Hospital management of severely malnourished children, a condition that affects many young children in South Africa. We hope that, in the future, other people might benefit from this study through improved understanding of these issues and how they can best be addressed. Once the project is completed however, you will be invited for the presentation of the results at a meeting in your local health facility/hospital.

Do I have to be in this research and may I stop participating at any time?

Your participation in this project is completely voluntary. You may choose not to take part at all. If you decide to participate, you may stop participating at any time. If you decide not to participate in this project or if you stop participating at any time, you will not be penalized.

Is any assistance available if I am negatively affected by participating in this study?

Although we do not envisage a situation whereby you will be negatively affected by participating in this project, in case where such a scenario occurs you will be referred to a qualified health practitioner for appropriate medical attention.

What if I have questions?

This research is being conducted by **Moise Muzigaba** from the University of the Western Cape. If you have any questions about the research study itself, please contact the following person:

Study Coordinator's Name: Moise Muzigaba

University of the Western Cape

Private Bag X17, Belville 7535

Telephone: (021)959- 9392

Cell: 0730651833

Email: mochemoseo@yahoo.co.uk

This research has been approved by the University of the Western Cape's Senate Research Committee and Ethics Committee.

Appendix 6: Participant information sheet for hospital Hospital staff- Xhosa

UNIVERSITY OF THE WESTERN CAPE

School of Public Health

Private Bag X 17, Bellville 7535, South Africa

Tel: +27 21-9592809, Fax: 27 21-9592872

A WHO Collaborating Centre for Research and Training in Human Resources for Health Development

Isihloko somsebenzi: Uphando lokuzalisekisa kwemiqago ka-WHO yokungondleki ngenxa yolwazi ngokungqamene neHIV/AIDS eMpuma Kapa.

Imida yophando

Olu luphando olwenziwa ngumfundi wePhD kunye noojingalwazi weSikolo seMpilo kaWonke-wonke /soLuntu eYunivesithi yaseWestern Cape. Siyakumema ukuba uthathe inxaxheba kolu phando lolwazi kuba umntwana wakho ulaliswe kwesi sibhedlele engondlekanga, ingxaki leyo eya kuphandwa kolu phando.

Senza uphando ngemiba engqamene nolawulo lwabantwana abangondlekanga esibhedlele, imeko echaphazela abantwana abaninzi eMzantsi-Afrika, ingakumbi eMpuma Kapa. Uninzi lwabantwana abalaliswa esibhedlele bachacha kade. Ngenjongo yokufumana iindlela zokukhawulezisa uchacho lwabantwana abondlekanga nokucutha isithuba sokulaliswa esibhedlele, simele ukuba nolwazi ngeengxaki ezibangela ukuchacha kade ngokuqinisekisa ukuba abasebenzi esibhedlele banalo ulwazi ngemigaqo esebenzayo yale mihla. Le migaqo iquka ukunika imilinganganiselo efanelekileyo yezinto ezibumanzi, ukutyisa okufanelekileyo nokulungisa intswelo yezimbiwa nokutya okomeleza izigulana. Ulwazi oluvela kolu phando luya kunceda abo basebenza kwezempilo bacwangise iinkqubo zokuphucula ulawulo lwabantwana abangondlekanga ezibhedlele.

Ukuthatha inxaxheba kwam kuya kuquka ntoni?

Uya kucelwa ukuba utyikitye ifomu yovumelwano esinika thina imvume yokuqinisekisa imo yeHIV yomntwana wakho simjonge umntwana wakho ngesithuba sonyango oluya kwenziwa kusetyenziswa iindlela zokunyanga ezicetyiswe ziingcali zezempilo. Abaphandi abaqeqeshiweyo baya kuhlola yonke imisebenzi engqameme nolawulo lwezigulana ezingondlekanga ngenjongo yokuqinisekisa ukuba kusetyenzwe ngendlela efanelekileyo. Ukuqinisekisa imo yeHIV kuya kwenziwa ngabongikazi abaqeqeshelwe lo msebenzi, abaya kutsala intwana yegazi (elilingane netispuni) lihlolwe ngumsebenzi welebhu oqeqeshiweyo. Uya kunikwa ingcebiso phambi nangemva kokuqinisekisa imo yeHIV yomntwana wakho.

Ukuthatha inxaxheba kwam kuya kupapashwa?

Siya kuzama kangangoko sinako ukuzigcina iinkcukacha zakho kunye nezomntwana wakho zibe yimfihlo. Ngenjongo yokugcina imfihlo, ngabaphando bodwa abaya kuba nolwazi ngeenkcukacha zenu. Aliyi kusetyenziswa igama lomntwana wakho; kuya kusetyenziswa amanani njengezazisi kuphela. Lwakugqityezelwa uphando, ulwazi / iinkcukacha ziya kugcinwa eYunivesithi yaseWestern Cape. Ukuba kubhalwa ingxelo okanye umhlathi ngolu phando, isazisi sakho asiyi kupapashwa. Ngokweemfuno kwezomthetho nemigangatho yomsebenzi, siya kuxela nayiphi na impatho embi okanye umonakalo onokwenzeka kumntwana, kuwe okanye kwabanye, kubantu okanye iziphathamandla ezifanelekileyo.

Yintoni ingozi yolu phando?

Akukho ngozi iyaziwayo ingqamene nokumvumela umntwana wakho athathe inxaxheba kolu phando.

Yintoni inzuzo yolu phando?

Olu phando alujongani nokukunceda wena ngobuqu, kodwa iziphumo zinganako ukunceda umphandi abe nolwazi ngemiba engqamene nolawulo esibhedlele lwabantwana abondlekanga, imeko embi echaphazela abantwana abaninzi abancinane eMzantsi Afrika. Sinethemba lokuba kwixesha elizayo, abanye abantu bangaba nenzuzo ngenxa yolu phando ngokuba nolwazi olongezelelweyo ngokungqamene nale miba nokulungiswa kwayo. Wakugqityezelwa umsebenzi, uya kumenywa kupapasho lweziphumo entlanganisweni eya kuba kho kwiziko lezempilo lengingqi yakho /esibhedlele.

Ndimelwe ukuthatha inxaxheba kolu phando okanye ndingayeka nangaliphi na ixesha?

Nguwe onika imvume yokuba umntwana wakho angathatha inxaxheba kolu phando. Ungakhetha ukuba angathathi nxaxheba. Ukuba ugqiba ukuba umntwana angathatha

inxaxheba,, ungayirhoxisa inxaxheba yakhe ngaliphi na ixesha ngaphandle kokunika isizathu. Ukuba ugqiba oku, wena nomntwana wakho aniyi kuchaphazeleka kakubi okanye nilahlekelwe yiyo nayiphi na inzuzo elungele nina. Ukukhathalela komntwana wakho akuyi kuchaphazeleka ngenxa yesigqibo sakho.

Imibuzo yam?

Olu phando lwenziwa ***nguMoise Muzigaba*** *weYunivesithi yaseWestern Cape. Ukuba unemibuzo ngokungqamene nophando olu, nceda uqhagamshele nalo mntu uchazwa ngezantsi:*

Igama lomququzeleli wophando:
Study Coordinator's Name: Moise Muzigaba
University of the Western Cape
Private Bag X17, Belville 7535
Telephone: (021)959- 9392
Cell: 0730651833
Email: mochemoseo@yahoo.co.uk
Olu phando luvunyelwe yiKomiti yoPhando neKomiti ejongene neNdlela yokuziPhatha yeYunivesithi yaseWestern Cape.

Appendix 7: Xhosa consent form for hospital Hospital staff

UNIVERSITY OF THE WESTERN CAPE

School of Public Health

Private Bag X 17, Bellville 7535, South Africa

Tel: +27 21-9592809, Fax: 27 21-9592872

A WHO Collaborating Centre for Research and Training in Human Resources for Health Development

IFOMU YOVUMELWANO

Uhlolo lokuzalisekisa kwemigaqo ka-WHO engqamene nokungondleki ngenxa yolwazi nge-HIV/AIDS eMpuma Kapa

Olu phando luchazwe ngolwimi endilwaziyo kwaye ndiyavuma ukuthatha inxaxheba kuba ndithanda. Imibuzo yam ngokungqamene nophando iphendulwe. Ndiyaqonda ukuba iinkcukacha ngesazisi sam aziyi kupapashwa kwaye ndingayirhoxisa inxaxheba yam ngaphandle kwesizathu ngaliphi na ixesha kwaye andiyi kuchapazeleka kakubi.

Igama lomthathi-nxaxheba

Utyikityo lomthathi-nxaxheba

Ingqina

Umhla

Ukuba unayo nayiphi na imibuzo malunga noluphando okanye ufuna ukuxela iingxaki obe nazo ngokungqamene nophando, nceda uqhagamshele nomququzeleli wophando:

Igama lomququzeleli wophando: Moise Muzigaba

University of the Western Cape

Private Bag X17, Belville 7535

Telephone: (021)959- 9392

Cell: 0730651833

Email: mochemoseo@yahoo.co.uk

Appendix 8: English consent form for hospital Hospital staff

UNIVERSITY OF THE WESTERN CAPE

School of Public Health

Private Bag X 17, Bellville 7535, South Africa

Tel: +27 21-9592809, Fax: 27 21-9592872

A WHO Collaborating Centre for Research and Training in Human Resources for Health Development

CONSENT FORM FOR THE HOSPITAL HOSPITAL STAFF

The WHO 10-step treatment modality for severe malnutrition in the context of HIV/AIDS comorbidity: An operational research in the Eastern Cape Province

The study has been described to me in a language that I understand and I freely and voluntarily agree to participate. My questions about the study have been answered. I understand that my identity will not be disclosed and that I may withdraw from the study without giving a reason at any time and this will not negatively affect me in any way. I also agree to keep everything that is said in the focus group discussion confidential

Participant's name.....

Participant's signature.....

Witness.....

Date.....

Should you have any questions regarding this study or wish to report any problems you have experienced related to the study, please contact the study coordinator:

Study Coordinator's Name: Moise Muzigaba

University of the Western Cape

Private Bag X17, Belville 7535

Telephone: (021)959- 9392

Cell: 0730651833

Email: mochemoseo@yahoo.co.uk

Appendix 9: Patient evaluation questionnaire

A: Study Number----------

Date of data collection----------

Name of data collector----------

Outcome----------

Hospital Hospital Evaluation Form

Complete the blank spaces. For 'status of child' and 'key dates', enter the information from the record. For the rest of the form, tick check boxes if actions were carried out correctly and cross if done incorrectly. Where check boxes are crossed provide an explanation in notes column. If the question is irrelevant (e.g. child not dehydrated) then enter -. If status is unclear (e.g. HIV) or it is unclear if a treatment was given (e.g. ORS after diarrhoeal stools), then enter?. When all the records have been reviewed, look again at those with ? and seek clarification (i.e. action not implemented or just not charted).

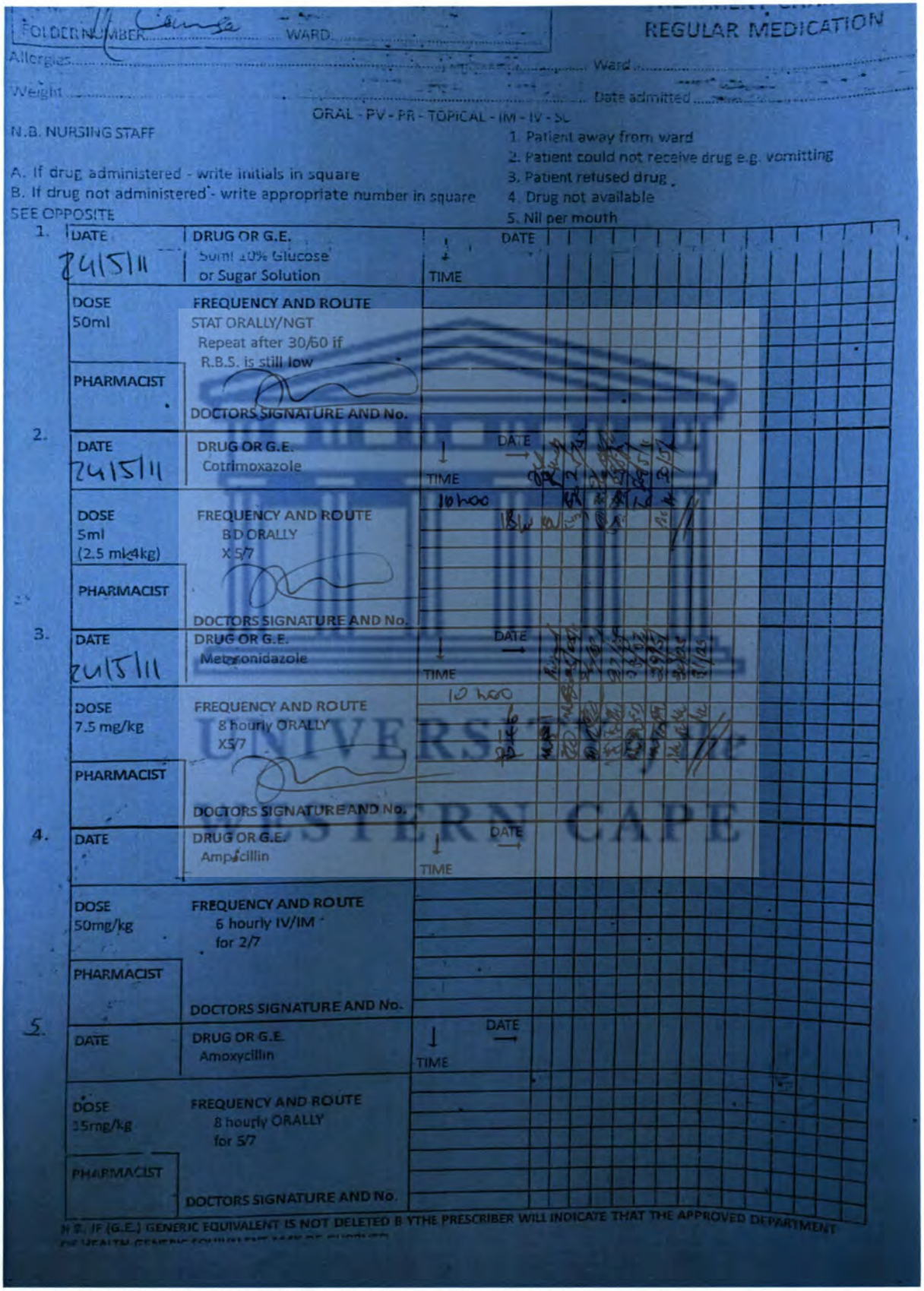
B	**HOSPITAL:**		
C	**Folder Number:**		
		Check	*Notes*
Q1	***Status of child*** *when admitted to current ward*		
Q2	Age (months)		
Q3	Weight (kg)		
Q4	Length/ height (cm)		
Q5	Mid upper Arm circumference(cm)		
Q6	Standard deviation of weight for height below median		
Q7	Oedema grade (0 + ++ +++)		
Q8	Dermatosis grade (0 + ++ +++)		

Q9	HIV status			
Q10	Was the child terminally ill?(write presenting signs and symptoms)			
	Started treatment in casualty or other ward *(state where, if applicable)*			
	Key dates			
Q11	Date admitted to current ward			
	Date discharged or died			
	Time of death *(if applicable)*			
Q12	Date of transition onto F100			
Q13	Date Orsol prescribed *(if applicable)*			
	Feeding			
Q14	Given 10% sucrose/ glucose within 10 minutes of arrival on ward			
Q15	Fed F75 as first feed			
Q16	Fed F75 within 30 minutes of arrival on ward			
Q17	Correct volume of F75 prescribed 3 hourly on day 1 -130/kg/day			
Q18	If child has gross oedema, reduce volume to 100 ml/kg//day			
Q19	NG tube correctly prescribed *(if intake <80% over 24h, or if intake is <80% for 3 consecutive feeds)*			
Q20	Total daily feed volume calculated correctly			
Q21	Transition onto F100 prescribed at right time *(hungry and reduced/minimal oedema)*			
Q22	Correct volume of F100 prescribed for transition (same amount as on F75)			
Q23	Volume of F100 increased per feed on day 3 of transition			
Q24	Total daily feed volume calculated correctly			
Q25	Diuretic not given for oedema			
	Antibiotics			
Q26	Antibiotics prescribed on day 1			
Q27	Appropriate course of antibiotics prescribed			
Q28	Cotrimoxazole prescribed if HIV +/ suspected			
Q29	Antibiotics administered as prescribed			
Q30	***If HIV positive, is ARV prescribed***			

	Electrolytes/Micronutrients			
Q31	K administered (e.g. as mineral solution mixture)			
Q32	Mg administered (e.g. as mineral solution mixture)			
Q33	Zn administered (e.g. as mineral solution mixture)			
Q34	Vitamin A prescribed on day 1			
Q35	Correct amount of Vitamin A prescribed			
Q36	Vitamin A prescribed on Days 2 and 14 only if eye signs			
Q37	Vitamin A administered			
Q38	5mg Folic Acid prescribed on Day 1			
Q39	Folic Acid administered daily			
Q40	Multivitamin prescribed daily			
Q41	Multivitamin administered			
Q42	Iron prescribed only at the beginning of the catchup phase			
Q43	Iron administered daily in the catchup phase			
	Rehydration			
Q44	IV fluids not prescribed or administered for rehydration except in shock			
Q45	Orsol prescribed for rehydration			
Q46	Orsol prescribed only if watery stools/ vomiting			
Q47	Correct volume of Orsol prescribed			
Q48	Orsol administered according to prescription			
Q49	Orsol alternated with F75 after first 2 hours			
Q50	Orsol only given up to 10 hours			
Q51	Child's respirations and breathing monitored at least hourly whilst on Orsol			
Q52	Watery stools are charted			
Q53	Orsol given after every watery stool			
	Treatment of shock			
Q54	Correct fluid (½ strength Darrows with 5% glucose, Ringer's with 5%glucose; ½N saline with 5%			
Q55	Correct volume prescribed (15ml/kg over 1h)			

Q56	Child's respirations and breathing charted at least every 10 minutes whilst on IV			
Q57	Changed to ORS after 2h			
	Blood transfusion			
Q58	Only given if Hb <4g% or 4-6g% with respiratory distress			
Q59	Correct volume prescribed (10ml/kg slowly over 3h)			
Q60	Furosemide prescribed to make room for blood (1mg/kg IV)			
	Monitoring			
Q61	Weight measured daily			
Q62	Weight accurately plotted on chart			
Q63	Starting weight same on nurses notes and weight chart			
Q64	More than 10g/kg/day weight gained whilst on F100 (NB record actual gain in *Notes*)			
	Study Information			
Q65	If HIV status unknown, pretest Counseling and date			
Q66	Consent form signed(state if refused)			
Q67	Date Blood taken for HIV test			
Q68	Date results received			
Q69	HIV outcome			
Q70	If HIV positive, state WHO HIV disease stage and presenting signs and symptomps			
	Have been gaining weight well(> 10 grams per kg per day) for at least 2 weeks			
	If the child has been discharged			
	Have the following criteria been followed?			
Q71	Completed the transition to catch up and eating well			
Q72	Have no oedema			
Q73	Have completed antibiotic treatment			
Q74	Received electrolytes and micronutritient for at least two weeks			
Q75	Up to date with immunizations			
Q76	Have RTHC that has been updated			

Appendix 10: Chemotherapy chart



FOLDER NUMBER ... WARD ... REGULAR MEDICATION

Allergies ... Ward ...

Weight ... Date admitted ...

ORAL - PV - PR - TOPICAL - IM - IV - SC

N.B. NURSING STAFF

A. If drug administered - write initials in square
B. If drug not administered - write appropriate number in square
SEE OPPOSITE

1. Patient away from ward
2. Patient could not receive drug e.g. vomitting
3. Patient refused drug
4. Drug not available
5. Nil per mouth

1. DATE 24/5/11 | DRUG OR G.E. 50ml ±0% Glucose or Sugar Solution | DATE → / TIME ↓
   DOSE 50ml | FREQUENCY AND ROUTE STAT ORALLY/NGT Repeat after 30/60 if R.B.S. is still low
   PHARMACIST | DOCTORS SIGNATURE AND No.

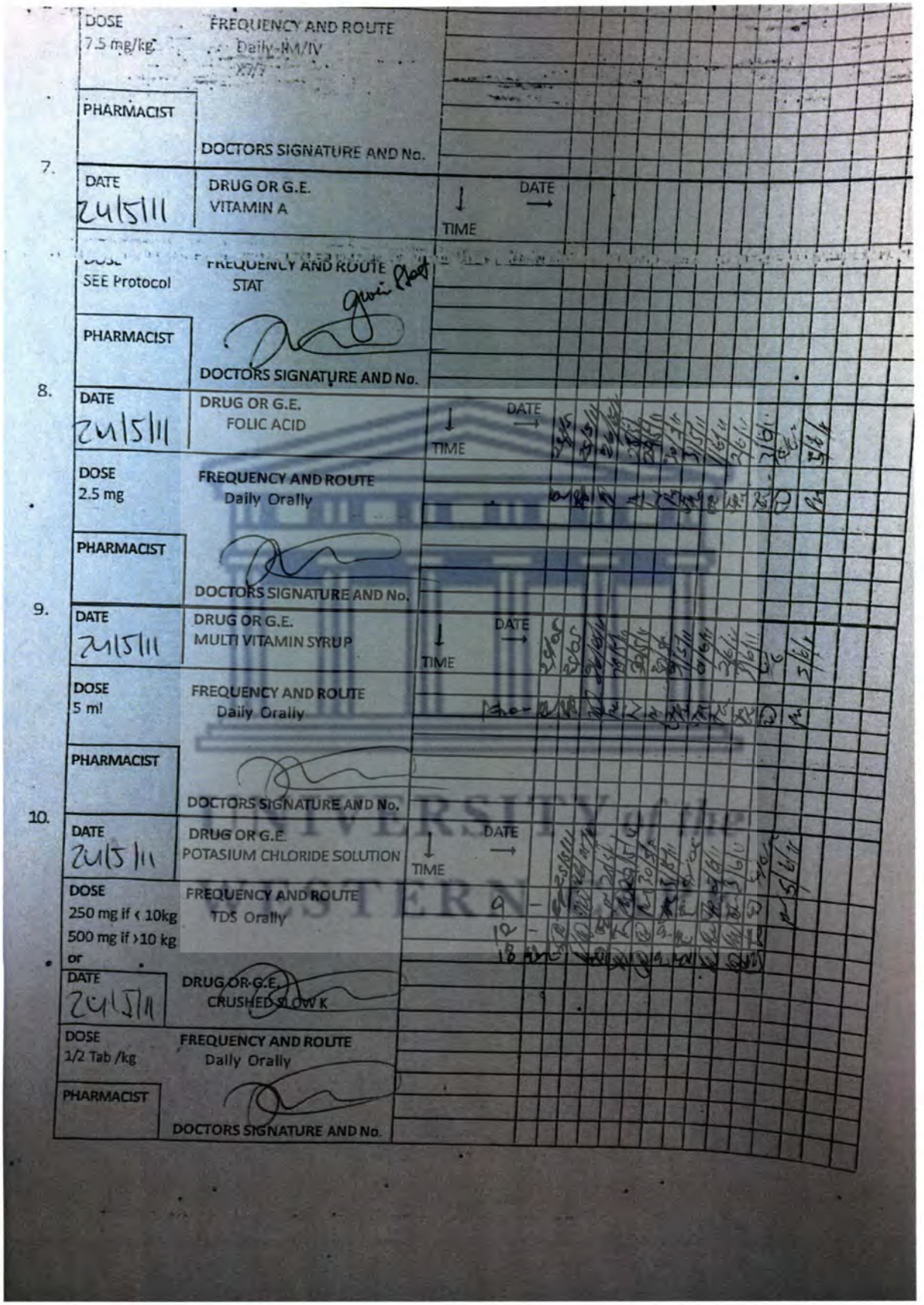
2. DATE 24/5/11 | DRUG OR G.E. Cotrimoxazole | DATE → / TIME ↓ 10h00
   DOSE 5ml (2.5 ml/4kg) | FREQUENCY AND ROUTE BD ORALLY X 5/7
   PHARMACIST | DOCTORS SIGNATURE AND No.

3. DATE 24/5/11 | DRUG OR G.E. Metronidazole | DATE → / TIME ↓ 10 h00
   DOSE 7.5 mg/kg | FREQUENCY AND ROUTE 8 hourly ORALLY X5/7
   PHARMACIST | DOCTORS SIGNATURE AND No.

4. DATE | DRUG OR G.E. Ampicillin | DATE → / TIME ↓
   DOSE 50mg/kg | FREQUENCY AND ROUTE 6 hourly IV/IM for 2/7
   PHARMACIST | DOCTORS SIGNATURE AND No.

5. DATE | DRUG OR G.E. Amoxycillin | DATE → / TIME ↓
   DOSE 15mg/kg | FREQUENCY AND ROUTE 8 hourly ORALLY for 5/7
   PHARMACIST | DOCTORS SIGNATURE AND No.

N.B. IF (G.E.) GENERIC EQUIVALENT IS NOT DELETED BY THE PRESCRIBER WILL INDICATE THAT THE APPROVED DEPARTMENT


DOSE
7.5 mg/kg
FREQUENCY AND ROUTE
Daily-PM/IV
PHARMACIST
DOCTORS SIGNATURE AND No.
7.
DATE
24/5/11
DRUG OR G.E.
VITAMIN A
TIME
DATE
SEE Protocol
STAT
PHARMACIST
DOCTORS SIGNATURE AND No.
8.
DATE
24/5/11
DRUG OR G.E.
FOLIC ACID
DOSE
2.5 mg
FREQUENCY AND ROUTE
Daily Orally
PHARMACIST
DOCTORS SIGNATURE AND No.
9.
DATE
24/5/11
DRUG OR G.E.
MULTI VITAMIN SYRUP
DOSE
5 ml
FREQUENCY AND ROUTE
Daily Orally
PHARMACIST
DOCTORS SIGNATURE AND No.
10.
DATE
24/5/11
DRUG OR G.E.
POTASIUM CHLORIDE SOLUTION
DOSE
250 mg if < 10kg
500 mg if >10 kg
or
FREQUENCY AND ROUTE
TDS Orally
DATE
24/5/11
DRUG OR G.E.
CRUSHED SLOW K
DOSE
1/2 Tab /kg
FREQUENCY AND ROUTE
Daily Orally
PHARMACIST
DOCTORS SIGNATURE AND No.

	DOSE 2.5 ml if <10 kg 5 ml if > 40 kg	FREQUENCY AND ROUTE Daily Orally	TIME
	PHARMACIST	DOCTORS SIGNATURE AND No.	
12.	DATE	DRUG OR G.E. FERROUS SULPHATE	DATE → ↓ TIME
	DOSE 5 ml	FREQUENCY AND ROUTE Dailly Orally (Catch up Phase)	10h00
	PHARMACIST	DOCTORS SIGNATURE AND No.	
13.	DATE (if no improve-ment after 48 hrs)	DRUG OR G.E. CHLORAMPHENICOL	DATE → ↓ TIME
	DOSE 25 mg/kg	FREQUENCY AND ROUTE 8 hrly IM/IV X 5/7	
	PHARMACIST	DOCTORS SIGNATURE AND No.	

NURSES SIGNATURE AGAINST INITIAL USED WITH MEDICATION					
INITIAL	NAME	INITIAL	NAME	INITIAL	NAME

Appendix 11: Feeding chart

Province of the
EASTERN CAPE
DEPARTMENT OF HEALTH

HOLY CROSS HOSPITAL
FEEDING CHART
MALNUTRITION

NAME: ....

Date:	Starter / Catch-up	Weight: .... kg	Amount to be given: .... ml

Feeds	Time given	Amount	Route	Left over	Vomited	Diarrhoea	Name
03:00			PO / NGT		yes / no	yes / no	
06:00			PO / NGT		yes / no	yes / no	
09:00			PO / NGT		yes / no	yes / no	
12:00			PO / NGT		yes / no	yes / no	
15:00			PO / NGT		yes / no	yes / no	
18:00			PO / NGT		yes / no	yes / no	
21:00			PO / NGT		yes / no	yes / no	
24:00			PO / NGT		yes / no	yes / no	

Date:	Starter / Catch-up	Weight: .... kg	Amount to be given: .... ml

Feeds	Time given	Amount	Route	Left over	Vomited	Diarrhoea	Name
03:00			PO / NGT		yes / no	yes / no	
06:00			PO / NGT		yes / no	yes / no	
09:00			PO / NGT		yes / no	yes / no	
12:00			PO / NGT		yes / no	yes / no	
15:00			PO / NGT		yes / no	yes / no	
18:00			PO / NGT		yes / no	yes / no	
21:00			PO / NGT		yes / no	yes / no	
24:00			PO / NGT		yes / no	yes / no	

Date:	Starter / Catch-up	Weight: .... kg	Amount to be given: .... ml

Feeds	Time given	Amount	Route	Left over	Vomited	Diarrhoea	Name
03:00			PO / NGT		yes / no	yes / no	
06:00			PO / NGT		yes / no	yes / no	
09:00			PO / NGT		yes / no	yes / no	
12:00			PO / NGT		yes / no	yes / no	
15:00			PO / NGT		yes / no	yes / no	
18:00			PO / NGT		yes / no	yes / no	
21:00			PO / NGT		yes / no	yes / no	
24:00			PO / NGT		yes / no	yes / no	

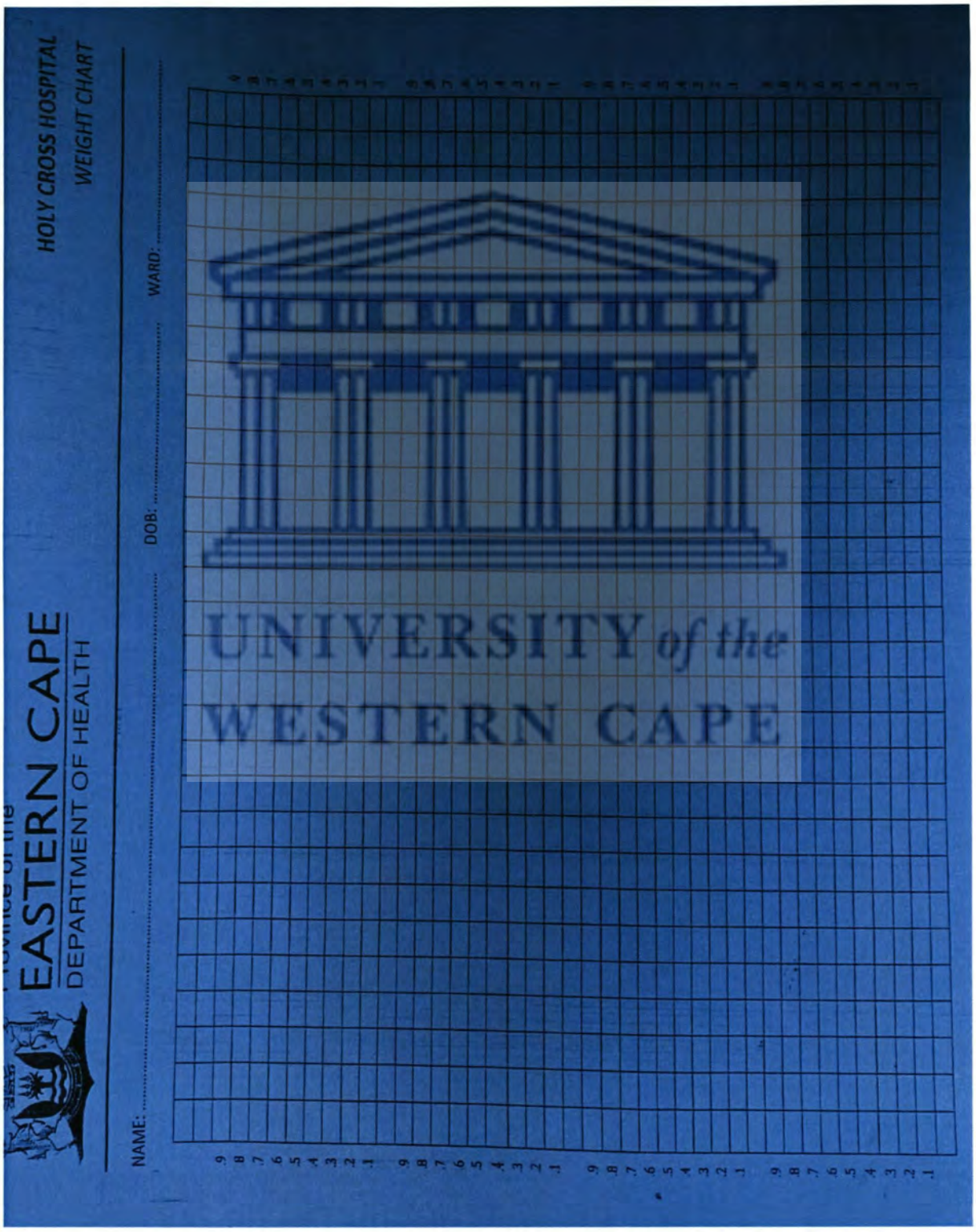
Appendix 12: Fluid discharge monitoring chart

Folder No……..

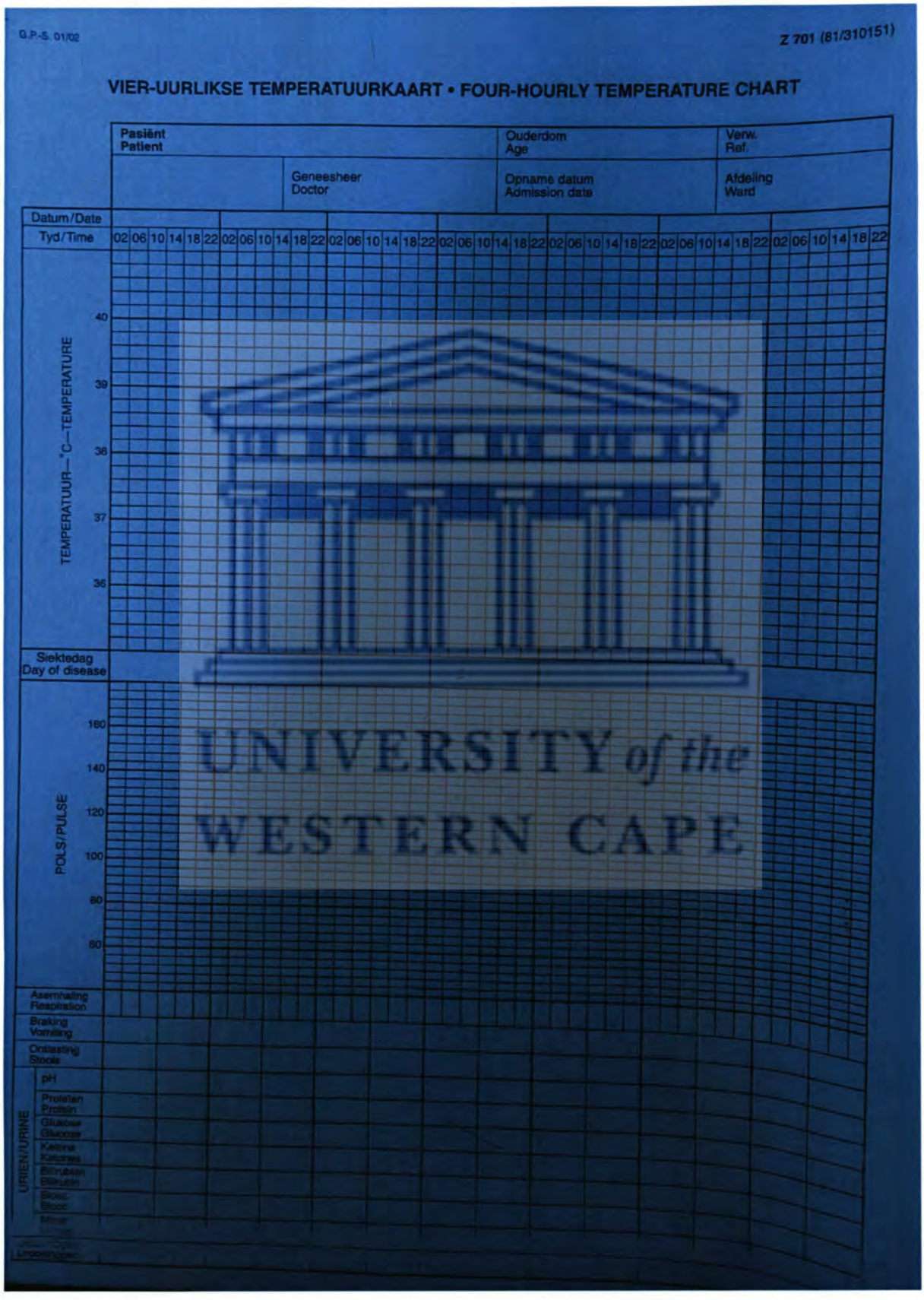
Name of patient …….. Ward……..

Date	Time	Urine in mls	Suction in Mls	Stool	Vomitus	Total	Signature

Appendix 13: Weight monitoring chart



Appendix 14: Temperature and Pulse Monitoring charts



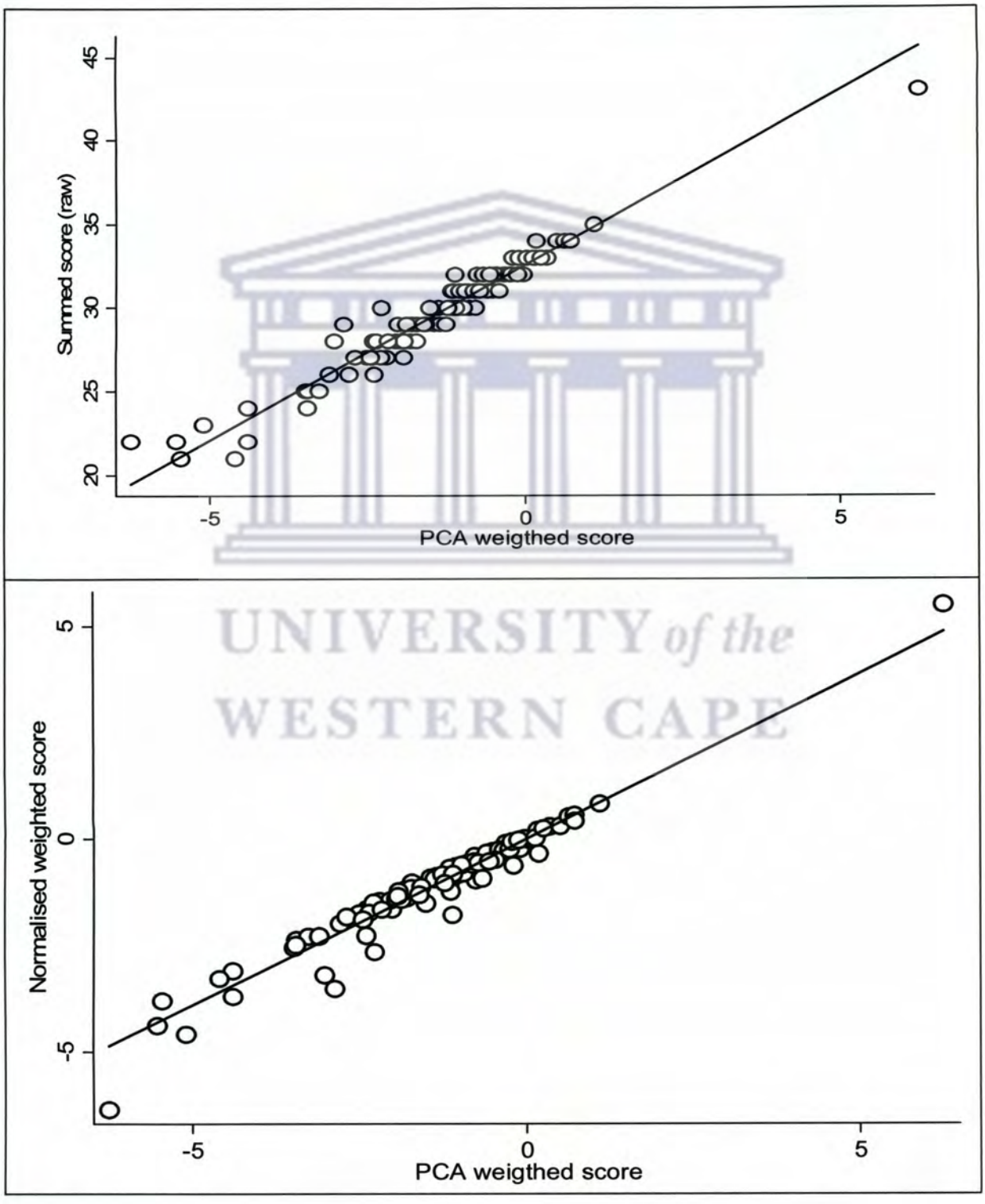
Appendix 15: ORSOL Chart

Folder No……..

Name of patient …….. Ward……..

Date	Time	Amount of ORSOL given in mls	Left overs in mls	Route	Signature

Appendix 16: Calculation of the quality of care composite score



Appendix 17: Data collection tool for the interrupted time series design

HOLY CROSS HOSPITAL

MONTHLY CASE FATALTY STATISTICS FROM JAN TO SEP 2010 Dec. 2010

Case fatality indicators	JAN	FEB	MAR	QRT1	APRIL	MAY	JUNE	QRT 2	JULY	AUG	SEP	QRT3	OCT	NOV	DEC	QRT 4	TOTAL
(A)Total ward admissions including severe malnourished	65	76	92	233	99	82	99	280	51	40	53	144	49	59	71	179	836
(B) Total ward submission on child support grant	31	50	51	142	47	43	38	128	30	20	26	76	39	30	49	118	464
Admission due to severe malnutrition	12	13	26	51	26	17	24	67	9	5	8	22	4	7	7+3	21	161
(a)malnourished without birth certificate	4	3	4	11	11	5	24	40	1	0	4	5	1	2	6	9	65
(B)Malnourished referred to home affairs	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0
(B)malnourished not getting child support grant	5	4	9	18	14	7	57	78	3	1	6	10	0	3	4	7	113
(B)malnourished referred to social development	5	7	9	21	0	5	5	10	0	0	6	6	0	1	4	5	42
Re-admission due to severe malnutrition	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0
(A)Re-admission no getting child support grant	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0
(B)Re-admissions getting child support grant	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total ward death [illegible]	[illegible]	15	16	48	19	16	19	54	2	4	8	14	7	5	8	20	136
(A)Deaths due to severe malnutrition [illegible]	[illegible]	3	6	14	[illegible]	[illegible]	[illegible]	18	0	2	[illegible]	3	0	1	3	4	39
[illegible]	[illegible]	0	1	2	4	0	8	12	0	0	1	0	2	0	0	0	15
[illegible]	[illegible]	3	0	3	0	3	1	4	0	0	0	0	4	14.3	0	0	0
[illegible]	[illegible]	15%	17%	21%	19%	20%	19%	19.3%	4%	[illegible]	15%	9.7%	7%	8.5	11.2%	11%	16%
[illegible]	[illegible]	23%	23%	27%	27%	41%	17%	27%	0%	40%	12%	13.0%	0%	14.3	30%	19%	24%

Appendix 18: Database for the interrupted time series design

Year	Month	Admissions due to SM	SM cases not getting child support grant	SM case referred to Social Services	Readmission cases due to SM	Total deaths due to SM	No of SM deaths within 24 hours of admission	Number of deaths due to SM & HIV positive	Ward Case fatality rate (%)	Case fatality rate due to SM (%)
2009	January									
	February									
	March									
	April									
	May									
	June									
	July									
	August									
	September									
	October									
	November									
	December									
2010	January									
	February									
	March									
	April									
	May									
	June									
	July									
	August									
	September									
	October									
	November									
	December									
2011	January									
	February									
	March									
	April									
	May									
	June									
	July									
	August									
	September									
	October									
	November									
	December									

2012	January									
	February									
	March									
	April									
	May									
	June									
	July									
	August									
	September									
	October									
	November									
	December									
2013	January									
	February									
	March									
	April									
	May									

Appendix 19: Data structure for the segmented regression analysis

Segmented regression variables					The four performance metrics			The denominator
Time	Discontinuation of the intervention	Time after intervention discontinuation	Observation		Total number of deaths due to SAM	Total number of deaths within 24 hours	Total number of deaths due to SAM and HIV infection	**Total admissions due to SAM**
1	0	0						
2	0	0						
3	0	0						
4	0	0						
5	0	0						
6	0	0						
7	0	0						
8	0	0						
9	0	0						
10	0	0						
11	0	0						
12	0	0						
13	0	0						
14	0	0						
15	0	0						
16	0	0						
17	0	0						
18	0	0						
19	0	0						
20	0	0						
21	0	0						
22	0	0						
23	0	0						
24	0	0						
25	0	0						
26	0	0						
27	0	0						
28	0	0						
29	0	0						
30	0	0						
31	0	0						
32	0	0						
33	1	1						

34	1	2						
35	1	3						
36	1	4						
37	1	5						
38	1	6						
39	1	7						
40	1	8						
41	1	9						
42	1	10						
43	1	11						
44	1	12						
45	1	13						
46	1	14						
47	1	15						
48	1	16						
49	1	17						
50	1	18						
51	1	19						
52	1	20						
53	1	21						

Appendix 20: List of senior FGC participants from Holy Cross Hospital

Province of the
EASTERN CAPE
DEPARTMENT OF HEALTH

HOLY CROSS HOSPITAL - Flagstaff - Eastern Cape
Private Bag X1001 - Flagstaff - 4811 - REPUBLIC OF SOUTH AFRICA
Tel.: +27 (0)39 252 3000/1 - Fax. +27 (0)39 252 3002 - E-mail: [illegible] - Website: www.ecdoh.gov.za

ATTENDANCE REGISTER

Chairperson: Moise Muzigaba

Scriber: Mss Gura

Date: 15/5/14

Venue: Holy Cross Hospital

Physical verification of Training site for Holycross Hospital

Feedback on Malnutrition

Surname & Initials	Designation	Contact No	Email Address	SIGNATURE
T.MAYIME	Pharmacist	076 308 7610	[illegible]	[illegible]
Nkwenkwe B	Amm	078 275 3091	—	[illegible]
Vuuwlu N.T	Anaesth	082 277 4596	N/A	[illegible]
MPOTO NP	Nm	073 116 2596	N/A	[illegible]
Mbusa M	management	0844557651	[illegible]	[illegible]
Ampondo	of malnutrition	073 301 7089	—	[illegible]
Gura N.P	Dietician	073 042 7160	[illegible]	[illegible]
Ntapu KET	MO	078 661 5162	[illegible]	[illegible]
Matodlung	Pm	0827959854		[illegible]
Zincle Z	Social Worker	0835135161	[illegible]	[illegible]

Appendix 21: List of senior FGD participants from St Patrick's Hospital

Province of the
EASTERN CAPE
HEALTH

St Patrick's Hospital • •Bizana • Eastern Cape
Private Bag X 531 • Bizana • 4800 • REPUBLIC OF SOUTH AFRICA
Tel: +27 (0)39 251 0236. • Fax: +27 (0)39 251 0266
Date: 16/05/2014

MEETING: Support visit & feedback on research conducted by UWC. VENUE: OPD BOARDROOM DATE: 16/05/2014

SURNAME & INITIAL	DESIGNATION	DEPARTMENT	CONTACT NO.	SIGNATURE
1. Ntezi G.L	Nsm	Nursing Admin.	0736725200	
2. Dr Khelifa Z	M.O	OPD.	0832081812	
3. N. Mpoth	SW	Soc Serv	0835071464	
4. N.C. Zim	Dietician	Dietetics	0786102086	
5. Nongwendu U	Pharmacist	Pharmacist	078 741 2626	
6. Jonas I.L	Pharmacist	Pharmacy	081 044 8481	
7. Banerji O	M.O	Paeds	# 5220	
8. Mbethe, Z	DDCS	Clinical Support	071 8139800	
9. Gwanyra N.	M/M/A	Admin.	0722791627	
10. Dobe Z	L.S.O	Procurement	039-2518236	
11. Zr Mavukwana	QAO	Quality	039-2510236	

Appendix 22: Letter of invitation – Holy Cross Hospital

FACULTY OF COMMUNITY AND HEALTH SCIENCES
School of Public Health

Private Bag X17, Bellville, 7535
South Africa
Tel: +27 (0) 21 959 3520/2809
Fax: +27 (0) 21 9592872
Website:
www.uwc.ac.za/publichealth

10 April 2014

The Manager
Holy Cross Hospital
Flagstaff, Eastern Cape Province

Dear Sir/Madam

REQUEST FOR A MEETING WITH CLINICAL AND MANAGEMENT STAFF: FEEDBACK ON A FOUR-YEAR RESEARCH INTO THE MANAGEMENT OF SEVERE MALNUTRITION AT HOLY CROSS HOSPITAL

My name is Professor Thandi Puoane and I am from the School of Public Health at the University of the Western Cape. For the past couple of years, my colleagues (Professor David Sanders and Professor Anne Ashworth) and I have been involved in an operational research at your facility to improve the management of severe malnutrition using the WHO 10-step guidelines.

This research project was concluded in 2013. We were able to arrive at some findings that we would like to share with the hospital as this is an ethical responsibility we have to observe. We also strongly believe that it would be beneficial to the hospital in terms of reflecting on hospital performance over the past few years and possibly chart a way forward as a collective. We believe it would be ideal to have two separate meetings: one with senior management and medical staff and the other with relatively junior staff in the management cluster as well as nurses.

In light of the above, we are kindly requesting that permission be granted to individuals from the following professional categories who are currently, or have been involved in the management of severe malnutrition to attend this meeting.

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1st Meeting on the 9th May, 2014
(Preferably from 8h00 to 9h00 AM)

As available:

1. Hospital CEO/Manager
2. Medical manager/superintendent
3. Medical officers
4. Junior and visiting doctors
5. Medical interns
6. Nursing service managers
7. Pharmacist

2nd Meeting on the 9th May, 2014
(Preferably from 11h00 to 12h00 AM)

As available:

1. Senior nurses
2. Paediatric nurses
3. Staff nurses
4. Junior nurses
5. Student nurses
6. Dietician
7. Food service manager

We trust that you will find this request agreeable and look forward to hearing from you soon

Sincerely,

Prof Thandi Puoane, B (Cur), MPH, Dr PH

Appendix 23: Letter of invitation – St Patricks Hospital

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10 April 2014

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St Patrick's Hospital
Bizana, Eastern Cape Province

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We trust that you will find this request agreeable and look forward to hearing from you soon.
Sincerely,

Sincerely,

Prof Thandi Puoane, B (Cur), MPH, Dr PH

Appendix 24: FGD guide

FOCUS GROUP DISCUSSIONS GUIDE 1

WELCOME

Introductions:

Greetings to the audience…

My name is ……..and I am with Professor ……..

We are researchers from the University of the Western Cape, School of Public Health

Presentation of the research - Brief overview.

FGD: Ground rules:

Before you participate, we will first ask you to sign a **consent form.** This form is a confirmation that you have agreed to participate in this discussion knowing well what it involves.

The discussion will only take place among those who sign the consent form.

You are asked to please remember the **following ground rules** during the discussion:

This is meeting is serves as a **feedback platform** to reflect on how the **hospital Hospital has performed** over the past few years.

As the nature of the research **is operational,** we hope to share some of the **factors** that led to the **successes and failures** discovered during **data analysis.**

Based on this information we hope to **develop a framework** that will **strengthen the successes and correct the failures.**

This is meant to be a **simple discussion** which will allow **everyone to share their ideas.** It is not meant to make any **judgment** about the **performance** of the hospital Hospital and the staff. Therefore you should **not feel shy or intimidated to talk** and you are encouraged to create a **conducing atmosphere** for the audience to feel at ease to share their views.

The discussion will be **recorded** using voice recorder to ensure that we adequately capture your ideas during the conversation. However, the comments from the focus group will remain **confidential** and your name will not be attached to any comments you make.

Everyone's opinion is important; we want to hear from each of you.

Let everyone talk but let's avoid talking at the same time.

Let's respect everyone's opinion.

Let's remember to turn off the cell phones.

FGD: The process:

I will be presenting the results one aspect after another and will interject with questions in between the results. You are free to interrupt me at any time where you need clarity or wish to comment on the results.

FOCUS GROUP QUESTIONS

Effect of HIV infection and disease stage on survival

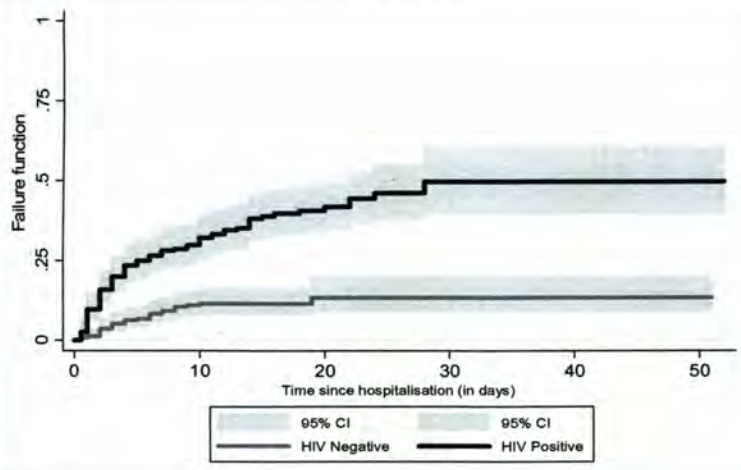
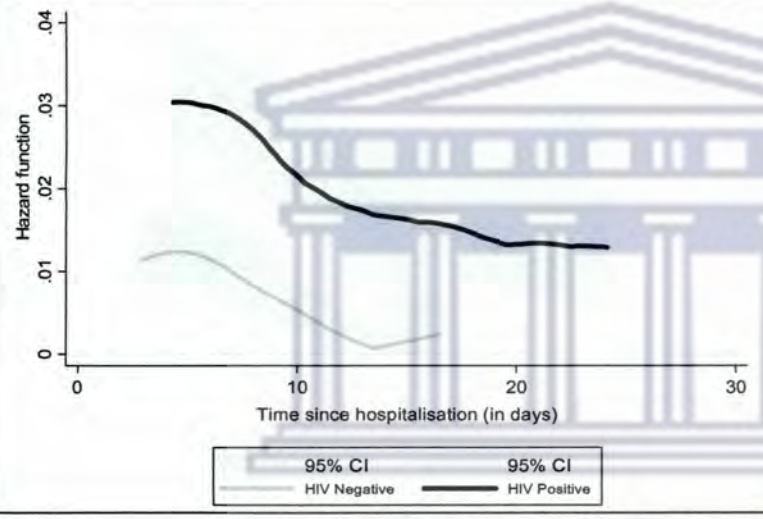
Focus

Comparing survival prospects among severely malnourished children with and without HIV infection

Potential effect of other clinical predictors (*HIV disease stage; duration of hospitalisation; rate of weight gain as an indicator of nutritional recovery; case severity on admission; as well as other clinical manifestations on admission which are directly or indirectly related to SAM*)

Hospital	Clinical classification of Severe Malnutrition								
	Marasmus		Kwashiorkor		Marasmic-Kwashiorkor		Total		
	n	(%)	n	(%)	n	(%)	n	(%)	*p* value
St Patrick's									
HIV Negative	15	22.7	41	62.1	10	15.2	66	100	
HIV Positive	44	56.4	20	25.6	14	17.9	78	100	*p <0.001*
Total	59	40.9	61	42.3	24	16.7	144	100	------
Holy Cross									
HIV Negative	48	25.0	98	51.0	46	23.9	192	100	
HIV Positive	66	55.9	22	18.6	30	25.4	118	100	*p <0.001*
Total	114	36.8	120	38.7	76	25.5	310	100	------

More HIV positive SAM cases were marasmic compared to their HIV negative counterparts
The reverse was true for cases that had kwashiorkor
For cases with marasmic-kwashiorkor there were no differences across HIV status

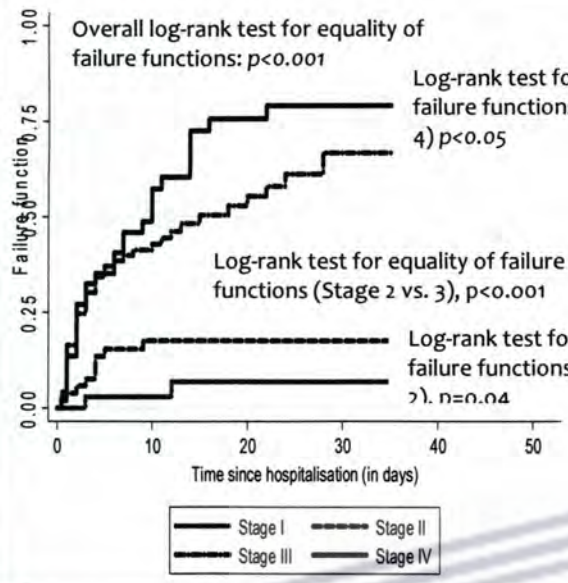
	HIV positive cases had worse survival prospects compared to their HIV negative counterparts HIV positive cases died sooner and in larger numbers than HIV negative cases
	Risk of death was consistently higher for HIV positive cases than HIV negative cases Higher risk in the period just after admission for both groups which then subsequently declined during the treatment period

In your own view and experiences dealing with SAM cases, what are the driving factors for such differences in mortality over and above HIV infection?

Please comment on the relevance of the WHO 10-step guidelines in alleviating case fatality rates in your facility over the past few years

What is your view regarding the effectiveness of the guidelines in addressing the differences in mortality between HIV infected and HIV uninfected SAM cases?

	Children who were at Stage 4 of HIV infection had significantly worst

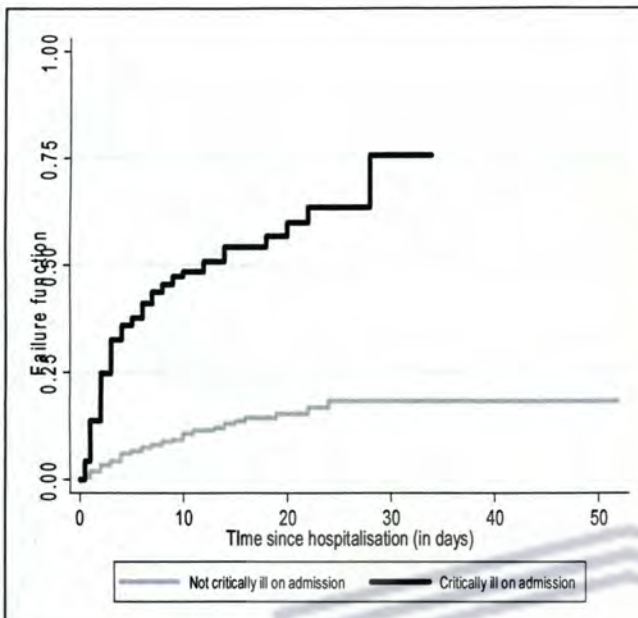
	survival prospects followed by those who were at Stage 3 Implies that the real threshold breach for higher risk of death was when cases were admitted at Stage 3 of HIV infection, followed by Stage 4

What are your views regarding the effectiveness of the guidelines in treating cases who are at different stages of HIV infection?

What about the role of antiretroviral therapy. To what extent or how does ART complement the guidelines at your facility?

Any other challenges you have encountered in relation to cases at different stages of infection?

	Of those who were admitted in a critical condition, about 25% only survived till the second day in the hospital Hospital compared to 1% of cases who were severely malnourished but were not



critically ill.
Factors classifying a case as critically ill on admission were 1. Depressed conscious state (prostration or coma), 2. Bradycardia, 3. Evidence of shock with or without dehydration and/or 4. Hypoglycaemia. Otherwise the case was not critically ill.
These clinical manifestations determined early death following admission

Thematic indicators of quality of care	n	Mean	SD	Min	Max	IEP [a,b]
Score for treatment of hypoglycaemia	454	13	1.3	5	14	[0,14]
Score for treatment of infection	454	3.7	0.76	1	4	[0,4]
Score for electrolyte imbalance & micronutrient deficiency	454	11.8	1.4	2	13	[0,13]
Score for management of rehydration	404	10.4	1.3	1	11	[0,11]
Score for treatment of shock	140	3.1	1.2	0	4	[0,4]
Score for blood transfusion	75	2.7	1.4	0	3	[0,13]
Score for patient monitoring	450	3.7	0.3	0	4	[0,4]
Score for appropriate patient discharge procedure	334	5.3	1.4	0	7	[0,7]

Quality of care was optimal overall except in the case of treatment of shock and patient discharge procedure/criteria. The quality of care varied periodically.

What are some of the factors that affect,

Effective treatment of shock

Patient discharge after full recovery

What has led to the quality of care not remained the same over time?

What are some of the organisational and structural factors that affect the quality of care in your view, in terms of implementation of the guidelines? Probe for

Financial

Human resource

Procurement of supplies and resources

Communication within the organisation

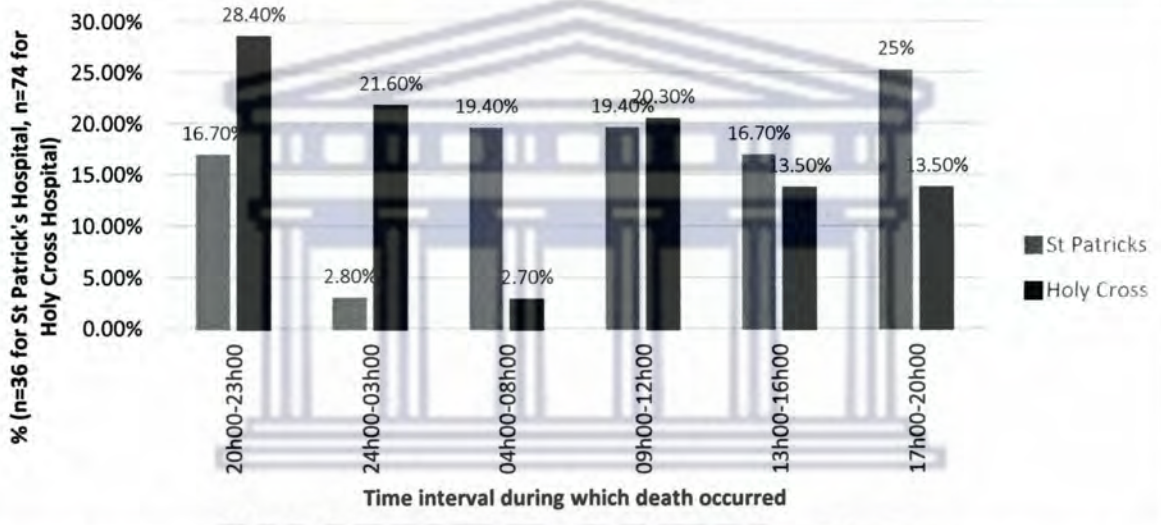
Support structures around the hospital Hospital (laboratory, blood banks)

Decision making channels

Interaction terms					Statistics		
			n*/N	HR#	95% CI		p
HIV (0=No, 1=Yes)	LRTI/TB (0=No, 1=Yes)	Critically Ill on admission (0=No, 1=Yes)			[Lower]	[Upper]	
			9/165	1			
0	0	1	9/35	4.83	1.92	12.18	0.001
0	1	0	3/35	1.55	0.42	5.71	0.513
0	1	1	8/15	14.64	5.64	38.01	<0.001
1	0	0	12/89	2.18	0.92	5.19	0.078

1	0	1	17/25	22.00	9.78	49.49	<0.001
1	1	0	20/39	9.86	4.49	21.68	<0.001
1	1	1	30/39	19.79	9.39	41.73	<0.001

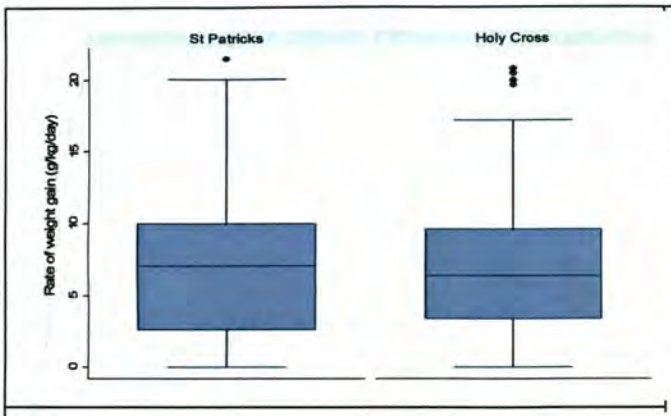
Cases who had LRTI's/TB and were critically ill at admission had 14 times higher hazard of death compared to those who had none
For SAM cases who were HIV positive and had LRTI's and/or TB, had only 9 times higher hazard of death
Cases who only had HIV infection and were critically ill on admission 22 times higher hazard of death compare to those who had none.
Important to consider these combinations to assess higher risk of death

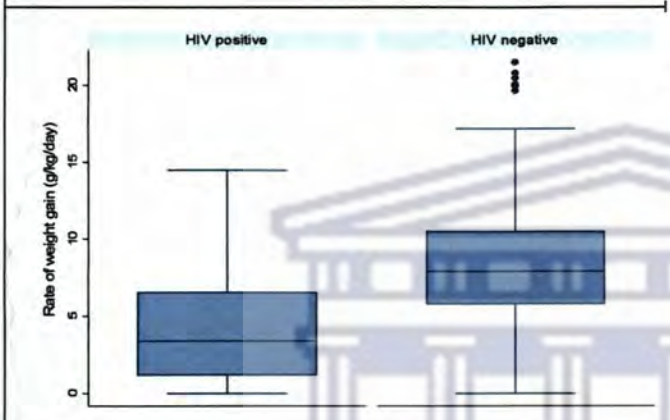


Most cases died between 20h00 and 23h00 (28.4%), followed by the period between midnight and 03h00 in the morning (21.6%)

What are the reasons for such patterns of death? Are they related to shortage of staff during these time intervals?

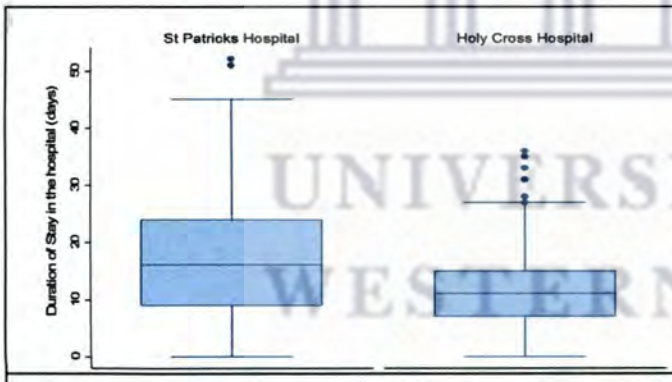
Duration of Hospitalisation and the Rate of Weight Gain

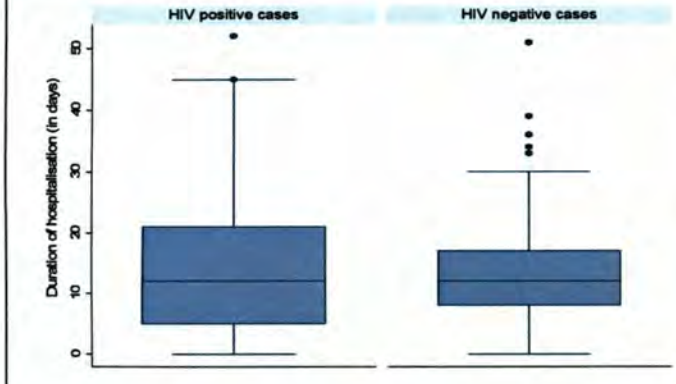




50% of cases achieved a rate of weight gain less than 7g/kg/day

Rate of weight gain among HIV positive cases was poorer (Median=3.6g/kg/day) than the rate of weight gain among HIV negative SAM cases (Median=7.5/kg/day)



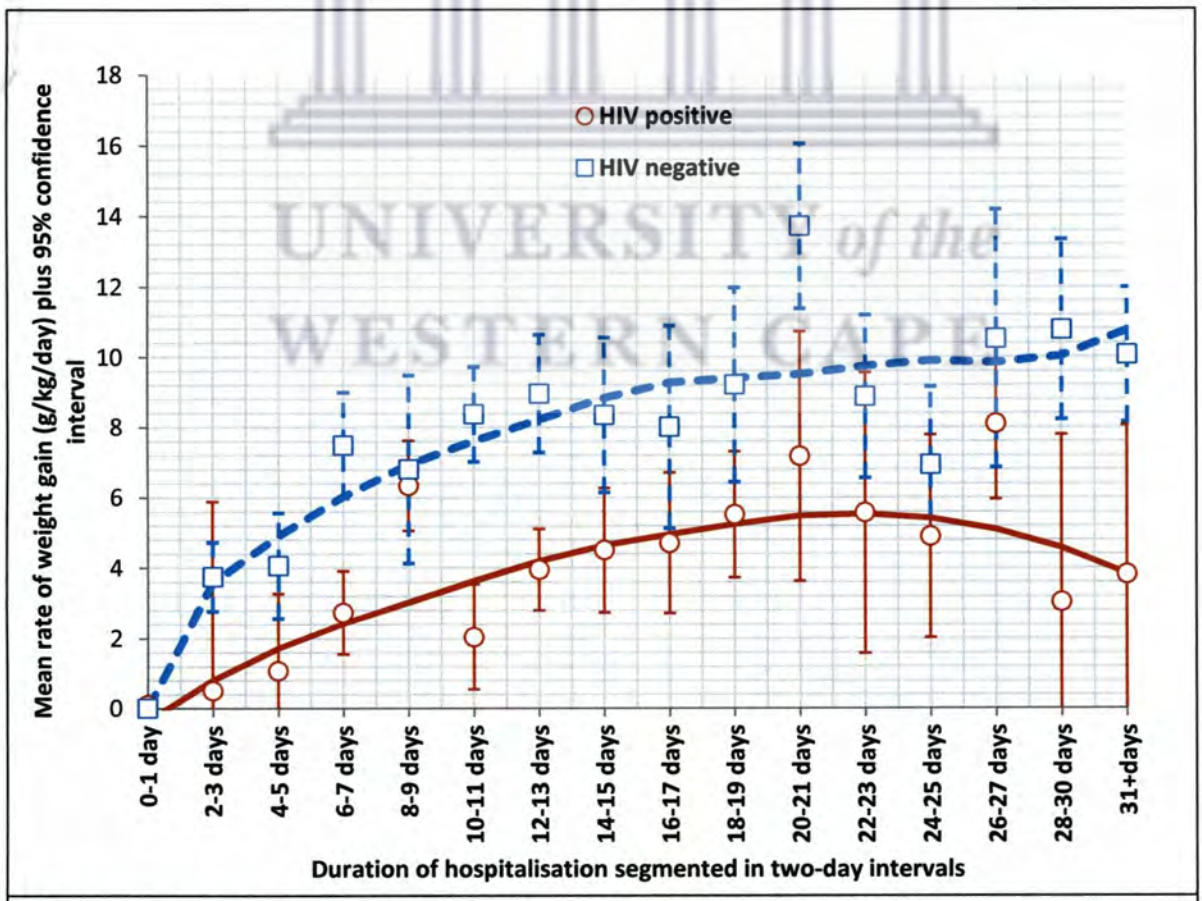


As shown in Figure #, the median duration of stay was longer at St Patrick's than at Holy Cross Hospital Hospital (16 and 11, respectively)

There was no difference in how long HIV positive SAM cases and their HIV negative counterparts spent in the hospital Hospital whilst on treatment

Results from the quality of care evaluation revealed that patients do not always get discharged after full recovery. Is this one of the reasons why duration of hospitalisation is similar between HIV positive and HIV negative cases?

What are some of reasons for early discharge of patients?



On average it took longer for HIV positive SAM cases to attain the same rate of weight gain as their HIV negative

counterparts within the same time frame

The rate of weight gain was much faster during the first few days following the stabilisation phase for both HIV positive and HIV negative cases, but level out almost after the 15th day post-stabilisation phase.

e.g. *in order for HIV positive SAM cases to attain a rate of weight gain of about 4g/kg/day following the stabilisation phase, they had to spend at least 15 days in the hospital, excluding the stabilisation period*

Clearly, HIV positive cases and their HIV negative alike need to stay longer in the hospital Hospital after the stabilisation phase to achieve optimal rates of weight gain. Unfortunately this has not been achieved.

What are some of the reasons for this shortfall?

What can be done to ensure that patients stay in the hospital Hospital while on treatment for a sufficient number of days until they attain full recovery?

What has been the greatest challenge to reduce CFRs to below 10% throughout this period?

Are there any other remarks you would like to share regarding the management of SAM at your facility?

Thanks you for your participation

We will use this information to develop a framework for strengthening the management of SAM in your hospital Hospital and we shall be sharing it with the hospital Hospital manager / CEO towards the end of the year